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THE ETIOLOGY OF INFANTILE ACQUIRED HEMIPLEGIA *

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INTRODUCTION

Hemiplegia in infancy is an unusual condition. Indeed, an analysis of the United States census report shows that the liability to hemiplegia in the first decade is less than one sixtieth of that in the seventh decade. Nevertheless, approximately seventy such hemiplegias are to be found in the records of the Harriet Lane Home among more than 50,000 case histories. Hemiplegia in adults is usually associated with hypertension, arteriosclerosis and syphilitic disease of the arteries. Hemiplegia in infancy results from very different factors. The acute hemiplegias of children usually occur under the age of 6 years, either during convalescence from some specific fever or without discoverable antecedent. The onset is febrile and is attended by focal or general convulsions. Delirium or stupor is present. Within a few hours or a day after the onset, paralysis is noted, almost invariably of hemiplegic distribution. In the next few days the child rapidly improves, but the hemiplegia is usually, although not invariably, permanent. More rarely death results, most often from a complicating pneumonia. Subsequently, the growth of the affected limbs is retarded, and various involuntary move-

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ments may appear on that side. Mental development is more or less affected. In about half of all cases epilepsy follows.

This brief description defines the clinical group with which this paper deals. Palsies due to heart disease, congenital defect of the brain, injuries at birth, postnatal traumatic palsies, cerebral neoplasms, meningitis and abscesses are excluded. Various names are applied to this syndrome. Polio-encephalitis, Marie-Strümpell encephalitis, Strümpell-Lichtenstern encephalitis and infantile meningo-encephalitis are the most common. Little is known about the etiology and not a great deal about the morbid anatomy, but several principal theories have been advanced. Abercrombie [1] claimed that embolism was the commonest process. Gowers [2] felt that venous thrombosis best explained the symptoms. Strümpell [3] suggested, in 1884, that a primary inflammatory process of the cortex was the initial lesion and that the virus was the same as that which causes poliomyelitis. Several years later,[4] he described two cases of the so-called hemorrhagic encephalitis in adults and claimed that this was the pathologic process involved in infantile hemiplegia. Taylor [5] holds similar views and has even attributed the postinfectious hemiplegias to a primary encephalitis which develops, he thinks, when the child's resistance is weakened by illness. Sachs [6] formerly maintained, with good reason, that vascular lesions were always found in these cases. More recently he has been inclined to admit that some cases may be due to encephalitis. Southard [7] and his co-workers have shown that pyogenic organisms may produce various cerebral lesions. He has termed this type of hemiplegia "bacterial apoplexy."

INFANTILE HEMIPLEGIAS FOLLOWING ACUTE INFECTIOUS DISEASES

PERTUSSIS

A great variety of symptoms referable to the central nervous system have been described in association with pertussis. Hemiplegias and other cerebral palsies constitute a considerable proportion of this group.

1. Abercrombie, J.: Brit. M. J. **1**:1323, 1887, and **1**:76, 1888.

2. Gowers, W. R.: Diseases of the Nervous System, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1907.

3. Strümpell, A.: Jahrb. f. Kinderh. **22**:173, 1884.

4. Strümpell, A.: Deutsches Arch. f. klin. Med. **47**:53, 1890.

5. Taylor, J.: Nervous Diseases in Childhood and Early Life, 1905.

6. Sachs, B.: Nervous Diseases of Children, New York, William Wood & Co., 1905.

7. Southard, E. E., and Sims, F. R.: A Case of Cortical Hemorrhages Following Scarlet Fever, J. A. M. A. **43**:789 (Sept. 17) 1904. Southard, E. E., and Keene, C. W.: Am. J. M. Sc. **129**:474, 1905. Southard, E. E., and Keene, C. W.: A Study of Brain Infections with the Pneumococcus, J. A. M. A. **46**:13 (Jan. 6) 1906. Southard, E. E., in Osler and McCrae, A System of Medicine, 1910, vol 7, p. 624. Bullard, W. N., and Sims, F. R.: Boston M. and S. J. **151**:647, 1904.

Thus, among the 120 infantile hemiplegias that Osler [8] reported in 1889, there were three that he considered sequels of pertussis. Freud and Rie [9] refer to fifteen similar cases. Schreiber,[10] ten years later, found records of thirty-eight cases in which cerebral lesions developed during pertussis, and in 1900, Hockenjas [11] found reports of forty-one cases in the literature, twenty-eight of which were hemiplegias. In Paul Valentine's thesis,[12] in 1902, there were included reports of six cases of paraplegia, sixteen cerebral monoplegias and forty hemiplegias, all of which were attributed to pertussis. These palsies are of two types, those which clear up rapidly without residuum and those which persist. Both usually develop during the active stage of the disease and often follow an especially severe paroxysm.

The anatomic basis of these conditions is fairly uniform. In all of Schreiber's ten cases, intracranial hemorrhage was found at autopsy. These hemorrhages were most frequent in the meninges. Hagenback's [13] nine autopsies revealed meningeal hemorrhage in two and intracerebral bleeding in seven. Hockenjas reported intracerebral hemorrhage in six of his eleven autopsies and meningeal hemorrhage in four. Rhein [14] collected reports of twenty autopsies, in 1905, in all of which intracranial bleeding had occurred during pertussis. It is well known that epistaxis, subconjunctival hemorrhage, hemorrhage in the orbit and from the upper respiratory passages sometimes occur after paroxysms. However, pathologic conditions of the brain other than hemorrhage may occur. Jarke [15] found many foci of inflammation and cellular infiltration of the vessel walls in his case of double hemiplegia which followed pertussis. Two large areas of softening were found in the cortex. Jacobson,[16] Heubner,[17] West,[18] Guibert,[19] Schreiber [10] and Baginsky [20] were unable to find any pathologic alterations in the brains of children who died soon after hemiplegia had developed. Rolleston [21] states that postmortem examination of the brains of children who have died with cerebral symptoms may reveal

8. Osler, William: The Cerebral Palsies of Childhood, 1898.
9. Freud, S., and Rie, O.: Beitr. z. Kinderh. **3**:195, 1891.
10. Schreiber, E.: Arch. f. Kinderh. **26**:1, 1899.
11. Hockenjas: Jahrb. f. Kinderh. **51**:425, 1900.
12. Valentine, Paul: Thesis, Paris, 1902.
13. Hagenback, in Gerhard's Handbuch 2, p. 568, 1877.
14. Rhein, J. A. W.: Spastic Diplegia Following Pertussis, J. A. M. A. **44**:697 (March 4) 1905.
15. Jarke: Arch. f. Kinderh. **20**:212, 1896.
16. Jacobson: Deutsche Ztschr. f. Nervenh. **4**:256, 1893.
17. Cited by Rhein (footnote 14).
18. West: Brit. M. J. **1**:157, 1887.
19. Guibert, cited by Schreiber (footnote 10).
20. Baginsky: Lehrb. d. Kinderkrankh., 1905, p. 160.
21. Rolleston, J. D.: Acute Infectious Diseases, New York, Physicians and Surgeons Book Company, 1925.

multiple fine hemorrhages in the cortex, local hyperemia and edema, or not any anatomic change at all. He believes that the process is toxic, and states that the palsies do not have any relation to the paroxysms. In the latter statement he is at odds with other clinicians of equal experience, and it is not probable that a unilateral paralysis would result from a general intoxication.

DIPHTHERIA

Hemiplegia after diphtheria is relatively uncommon, but numerous cases have been described. One of the first cases to be published was included in the Second Report of the Medical Officer of the Privy Council, by Sir William Gull,[22] in 1859. Another case was reported by Humphrey [23] in 1863. Rosenthal [24] published a similar case in 1885, and William Hunter [25] another three years later. Soon afterward, Wohlgemuth [26] added one and Woollacott [27] two more examples of hemiplegia complicating diphtheria. The last were the only cerebral palsies that occurred in 4,000 consecutive cases of diphtheria. Osler's series of 120 infantile hemiplegias did not contain any that were related to diphtheria. In 1898, Slawyk [28] was able to discover reports of fifty cases in the literature. In the next few years, several cases were reported by Mariottini,[29] Teillais [30] and Knoepfelmacher.[31] In 1905, Rolleston [32] abstracted the reports of the cases on record and found sixty-five in all. He added two of his own, which were the only ones that had occurred among 4,407 cases of diphtheria treated in the Grove Fever Hospital since its opening in 1899. In 1910, H. M. Thomas [33] gave diphtheria as the cause of four out of ninety-three acquired infantile hemiplegias. In 1913, Rolleston [34] presented reports of four additional cases of postdiphtheritic hemiplegia, one of which lasted only three hours. Dynkin,[35] Leede,[36] Mollet,[37] Auer [38] and Randegger [39]

22. Gull, William: Second Report of the Medical Officer of the Privy Council, 1859.
23. Humphrey, G. M.: Brit. M. J. **2**:3, 1863.
24. Rosenthal: M. Times & Gaz. August 15, 1885.
25. Hunter, W.: Scottish M. J. **3**:540, 1889.
26. Wohlgemuth: Abstr. in Neurol. Zentralbl. **17**:971, 1898.
27. Woollacott: Lancet **2**:1217, 1899.
28. Slawyk: Charité-Ann. **23**:385, 1898.
29. Mariottini: Quoted in Rev. neurol. 1899, p. 541.
30. Teillais: Abstr. in Rev. neurol. **12**:836, 1905.
31. Knoepfelmacher: Mitt. d. Gesellsch. f. inn. Med. u. Kinderh. **4**:40, 1905.
32. Rolleston, J. D.: Rev. Neurol. & Psychiat. **3**:722, 1905.
33. Thomas, H. M., in Osler and McCrae: A System of Medicine, New York, Oxford University Press, 1910, vol 7, p. 359.
34. Rolleston, J. D.: Clin. J. **42**:12, 1913.
35. Dynkin, A. L.: Jahrb. f. Kinderh. **78**:267, 1913.
36. Leede, W.: Ztschr. f. Kinderh. **8**:88, 1913.
37. Mollet, A.: Thesis, Paris, 1913-1914, no. 264.
38. Auer, E. M.: New York M. J. **101**:956, 1915.
39. Randegger, G. F.: Rev. de clin. pediat. **13**:488, 1915.

published reports of several cases in the next two years. In 1916, Rolleston [40] described two new cases in which the hemiplegia lasted less than twenty-four hours. He again summarized the literature and found that the total had risen to ninety-six. At that date eight hemiplegias had been observed among 11,313 cases of diphtheria in the Grove Fever Hospital. Ironsides and Hinds Howell [41] have recently presented the report of an additional case before the Royal Society of Medicine of London.

About twenty-one autopsies are on record. In one case an abscess was found; in one case, cerebral hemorrhage; in one case, pial edema associated with uremia; in three cases, cerebral thrombosis; in thirteen cases, cerebral embolism, and not any demonstrable pathologic alterations in one case. A case reported by Southard and Keene [42] was the result of a secondary septicemia with *Staphylococcus aureus* which caused multiple hemorrhagic inflammatory lesions in the brain. The case of Ironsides and Hinds Howell, which did not come to autopsy, showed evidences of multiple hemorrhages throughout the body. The diagnosis of "hemorrhagic encephalitis" was made. Rolleston [43] has observed embolic occlusion of the basilar artery with extension of the clot to the circle of Willis. The diphtheritic infection was severe in all of these cases, and polyneuritis and albuminuria were almost invariable. Dilatation of the heart, irregular pulse and enlargement of the liver were present in most instances. There were evidences of embolism of the abdominal viscera in several cases. Thus, it seems clear that the persistent hemiplegias are in most cases the result of cerebral embolism, but the cause of the transient palsies is less certain. Rolleston is inclined to attribute them to minute emboli or to uremic intoxication rather than to vascular spasm which has been suggested. He refers to a paper by Achard and Levi [44] in which these authors describe transitory cerebral palsies due, they claim, to minute emboli from the heart. Cassel [45] attributed the hemiplegia in his case to uremia. Arteries other than the cerebral may be involved in diphtheria. Thus, in 1910, Rolleston [46] described eleven cases of gangrene of the extremities which followed diphtheria, and Robbins [47] was able to collect reports of twenty-five similar cases in 1918.

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40. Rolleston, J. D.: Rev. Neurol. & Psychiat. **14**:145, 1916.

41. Ironsides, R., and Hinds Howell, C. M.: Proc. Roy. Soc. Med., section of Diseases of Children, **19**:3, 1925.

42. Footnote 7 (second reference).

43. Rolleston, J. D.: Rev. Neurol. & Psychiat. **13**:373, 1915.

44. Achard and Levi: Bull. et mém. Soc. méd. d. hôp. de Paris, 1897, vol. 3, series 14.

45. Cassel, J.: Arch. f. Kinderh. **11**:1, 1890.

46. Rolleston, J. D.: Brit. J. Dis. Child. **7**:529, 1910.

47. Robbins: M. Rec. **94**:620, 1918.

OTHER ACUTE INFECTIOUS DISEASES

Hemiplegia after scarlet fever is even more rare than after diphtheria. De Haen is credited by Imbert-Goubeyre [48] with publishing the history of a case of postscarlatinal hemiplegia complicated by aphasia as early as 1760. Scattered case reports have appeared in the literature since then. Conde,[49] in 1857, Addy,[50] in 1875, Bernhardt [51] and Alexeff,[52] in 1885, Taylor,[53] in 1887 and Fürbringer,[54] in 1889, each published one or more case reports. In 1898, Osler included in his 120 infantile hemiplegias seven that followed scarlet fever. Dejerine,[55] in 1891, Neurath [56] and Montgomery,[57] in 1900, Southard and Sims [7] in 1904, Baginsky [20] in 1905, and Luukonen,[58] in 1907, reported numerous additional cases. In 1908, Rolleston [59] summarized the literature on the subject and found reports of sixty-six cases of postscarlatinal hemiplegia in all, including three cases of his own. He emphasized the extreme rarity of the condition and stated that among 10,781 patients having scarlet fever, treated in the Grove Fever Hospital, only three hemiplegias had been observed. De la Chappelle [60] reported an instance of embolic hemiplegia that occurred during convalescence from scarlet fever in 1910. H. M. Thomas did not include scarlet fever among the etiologic factors in his collection of ninety-three hemiplegias acquired in the first decade. In most cases the paralysis appeared after the first week of the disease, and in many cases the statement is made that the weakness came on during convalescence. Little is known about the anatomic basis of these hemiplegias. Autopsy has been performed in only seven cases during the early stages. Intracerebral hemorrhage was found in three of these, embolism in two, and thrombosis in one. In one case there were multiple extravasations in the cortex and some inflammatory foci in relation to the vessels. *Staphylococcus aureus* was found in the blood and viscera. Of twenty-eight cases which did not come to autopsy the assigned cause was uremia in five, hemorrhage in five, thrombosis in five and embolism in twelve. Rolleston believes that the diagnosis of uremic palsy is justified in these cases because there was

48. Imbert-Goubeyre: Gaz. méd. de Paris, 1863.
49. Conde: Trans. College Physicians of Philadelphia **8**:137, 1857.
50. Addy: Lancet **1**:643, 1875.
51. Bernhardt: Virchows Arch. f. path. Anat. **102**:26, 1885.
52. Alexeff: Arch. f. Kinderh. **24**:319, 1898.
53. Taylor, F.: Guy's Hosp. Rep. **23**:15, 1878.
54. Fürbringer: Deutsche med. Wchnschr. **25**:67, 1889.
55. Dejerine, J.: Arch. de physiol., 1891, p. 661.
56. Neurath, R.: Neurol. Zentralbl. **19**:316, 1900.
57. Montgomery, E. B.: Pediatrics **9**:110, 1900.
58. Cited by Rolleston (footnote 59).
59. Rolleston, J. D.: Rev. Neurol. & Psychiat. **6**:530, 1908.
60. De la Chappelle, A.: Arb. a. d. path. Inst. zu Helsingfors **3**:57, 1910.

severe nephritis and the palsy disappeared promptly and completely. A case of "hemorrhagic encephalitis" described by Toomey, Dembo and McConnell [61] as a sequel of scarlet fever may be mentioned here for the light it throws on the pathologic process, although a complete hemiplegia did not develop. In this case multiple cerebral hemorrhages were found in the brain with hyaline degeneration and thromboses of the small vessels. Inflammatory foci were not found. Congestion of the spleen and petechial hemorrhages in the muscle of the heart were the only other observations. It must be noted that phlebitis and gangrene of the extremities indicating involvement of the peripheral vessels also sometimes follows scarlet fever. Huenekens and Siperstein [62] have discussed this subject recently.

Pneumonia in children may be followed by hemiplegia in rare instances. Sachs and Peterson [63] give six examples among eighty-three infantile hemiplegias in all. Gowers mentions one and Thomas one. Aufrecht [64] has described two cases with complete recovery. Withington [65] also describes a similar case and refers to numerous cases in the literature. Suckling [66] observed postpneumonic hemiplegia due to thrombosis of the circle of Willis in a young girl. Southard and Keene [67] and Bullard and Sims [68] reported numerous autopsies on patients dying with cerebral lesions in the course of pneumonia. In some cases they found numerous punctate hemorrhages in the cortex and inflammatory foci surrounding thrombosed vessels. The pneumococci were demonstrated in the tissues of the brain. Lesieur and Froment [69] say that some pneumonia hemiplegias are caused by thrombosis of the cerebral vessels, some by a pneumococcic encephalitis, and in some instances anatomic changes have not been found at autopsy. Holt and Howland [70] say that in about 25 per cent of a large series of cases of bronchopneumonia in children, positive blood cultures were obtained. Pneumococci were found most often, but other organisms were not infrequent.

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61. Toomey, J. A.; Dembo, L. H., and McConnell, G.: Acute Hemorrhagic Encephalitis, Am. J. Dis. Child. **25**:98 (Feb.) 1923.

62. Huenekens, E. J., and Siperstein, D. M.: Postscarlatinal Nephritis, Am. J. Dis. Child. **26**:447 (Nov.) 1923.

63. Sachs, B., and Peterson, F.: J. Nerv. & Ment. Dis. **17**:295, 1890.

64. Aufrecht: Arch. f. Kinderh. **11**:241, 1889-1890.

65. Withington, C. F.: Am. J. M. Sc. **147**:203, 1914; Medical and Surgical Report of Boston City Hospital, 1913; Boston M. & S. J. **168**:945, 1913.

66. Suckling, cited by Withington (footnote 65).

67. Footnote 7 (third reference.

68. Footnote 7 (fifth reference).

69. Lesieur and Froment: Rev. de méd., October, 1911.

70. Holt, E., and Howland, J.: Diseases of Infancy and Childhood, ed. 7, New York, D. Appleton & Co., 1919.

In 1907, Smithies [71] collected the reports of forty-three cases of hemiplegia which followed typhoid fever. Among these were nine cases in children under the age of 10 and four under the age of 5. Williams [72] again searched the literature in 1912, but did not find any additional cases in children. H. M. Thomas attributed five of his ninety-three infantile hemiplegias to typhoid fever, but Sachs and Peterson and Osler did not observe any examples of this rare condition. Thrombosis of the cerebral arteries has been found in every instance in which autopsy has been performed. In only one of the nine infantile cases was an autopsy performed.

Measles is sometimes complicated by hemiplegia. Sachs and Peterson include two cases which followed measles, and Thomas and Osler each four cases. In 1890, Freud and Rie found reports of twelve cases in the literature. We have been unable to discover any record of postmortem examination while the lesions were still fresh, so the anatomic basis of this complication of measles is unknown. However, thrombosis of the peripheral arteries is not unknown in severe cases of measles, and Hishon [73] was able to find twelve cases of gangrene of the legs following measles in 1925. According to Rolleston,[21] "encephalitis" is more frequent after measles than after any other acute exanthem. The so-called hemorrhagic encephalitis is sometimes found at autopsy. Winnicott and Gibbs [74] report an instance of this condition which followed measles. The clinical picture indicated a diffuse or disseminated process in the nervous system, and hemiplegia is unusual. In contrast to the hemiplegias, which are generally late complications, measles encephalitis occurs at the height of the disease.

Mumps meningitis is not uncommon in large epidemics, but hemiplegia is exceedingly rare. Nevertheless, Marie,[75] Putnam,[76] Gowers and Finlay [77] each have described cases of hemiplegia in children which followed a severe attack of mumps. None of these cases resulted fatally, so that the morbid anatomy is unknown. A mumps "encephalitis" is also described. Recovery is usually complete, but one of the authors has observed a case in which oculomotor palsies and a supranuclear facial weakness persisted.

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71. Smithies, Frank: Hemiplegia as a Complication in Typhoid Fever, J. A. M. A. **49**:389 (Aug. 3) 1907.

72. Williams: Am. J. M. Sc. **143**:677, 1912.

73. Hishon, D. J.: Proc. Roy. Soc. Med., Section of Diseases of Children **19**:35, 1926.

74. Winnicott, D. W., and Gibbs, N.: Brit. J. Child. Dis. **23**:107, 1926.

75. Marie, P.: Progrès méd., September 5, 1885.

76. Putnam, J. J.: J. Nerv. & Ment. Dis. **24**:1, 1897.

77. Finlay, G.: Glasgow M. J. **65**:50, 1906.

A case of hemiplegia associated with varicella has been reported by Gordon,[78] and Southard and Lucas [79] observed a monoplegia as a sequel to chickenpox. In Gordon's case there was hematuria and nitrogen retention, and it is possible that the hemiplegia resulted from the condition of the kidneys. Sachs and Peterson attribute a case of hemiplegia in a child to smallpox, and Freud and Rie collected reports of three cases of the same nature, in one of which autopsy showed softening of the whole hemisphere. Freud and Rie, Osler and Thomas all have observed cases in which hemiplegia followed vaccination against smallpox. In recent years considerable evidence has been accumulated to show that encephalomyelitis may occur in the course of variola, vaccinia and varicella. In contrast to most of the hemiplegias under discussion, these conditions seem to be specific effects of the primary virus. It is planned to report several cases of this nature in a later publication.

Gowers, Osler, Sachs and Peterson, and Thomas all include one or more cases of infantile hemiplegia which followed dysentery. It is not uncommon for a hemiplegic weakness to develop in the course of Sydenham's chorea. This weakness is transient and clears up without any residuum. Persistent hemiplegias are not unknown, however; Thomas has reported a case of this nature, and West [80] and Jordan [81] have added two more. Although many cases of postinfluenzal "hemorrhagic encephalitis" causing hemiplegia in adults are described in German medical literature, we have been able to find only a single instance in which influenza in a child was followed by hemiplegia. Batten and Prickett [82] demonstrated the autopsy material in this case before the Clinical Society of London, in 1900. The cortex showed multiple small hemorrhages and thromboses of the smaller vessels. There was an intense perivascular cellular infiltration. The authors believed that this case was an example of cerebral Heine-Medin disease.

INFANTILE HEMIPLEGIAS IN APPARENTLY HEALTHY CHILDREN

We have just discussed the hemiplegias that are associated with the exanthems and other acute infectious diseases of early life. In such cases the etiology is relatively clear. Another group of equal or greater size develops without any such preceding illness. Gowers has stated that five eighths of all infantile hemiplegias are apparently

78. Gordon, M. B.: Acute Hemorrhagic Nephritis and Acute Hemorrhagic Encephalitis Following Varicella, Am. J. Dis. Child. **28**:589 (Nov.) 1924.

79. Southard, E. E., and Lucas, W. P.: Boston M. & S. J. **169**:341, 1913; **166**:323, 1912.

80. Cited by Freud and Rie (footnote 9).

81. Jordan, W.: Proc. Midland M. Soc., December 13, 1911.

82. Batten, F. E., and Prickett, M.: Tr. Clin. Soc. London **23**:157, 1900.

primary. Osler could not find a cause for eighty-nine of a total of 120 cases. Thomas, and Sachs and Peterson could not discover the etiology in approximately half their cases. It is the occurrence of these hemiplegias in apparently healthy children, in whom there is not any demonstrable disease of the cardiovascular system, that has led to the general belief in the primary encephalitis which Strümpell postulated. However, the clinical picture is essentially identical with that presented by the postinfectious hemiplegias, and Strümpell's hypothesis still rests on insufficient anatomic evidence. In the following sections various possible etiologic factors will be considered.

RELATION TO POLIOMYELITIS

In 1884, Strümpell [3] suggested that the hemiplegias with fever and sudden onset in childhood were due to a primary encephalitis of the cerebral cortex and that the virus concerned was the same as that which causes poliomyelitis. He further suggested that the term polioencephalitis be applied to these cases of cerebral paralysis to indicate their etiologic identity with the cases of spinal paralysis. Strümpell's conclusions were based on the clinical similarities of the two conditions. He did not have any anatomic evidence to offer.

In support of Strümpell's theory that infantile hemiplegia is caused by the virus of poliomyelitis, it may be mentioned that Pasteur,[83] Moebius,[84] Medin,[85] Buccelli,[86] Hoffman,[87] Schlesinger [88] and Krause [89] have reported cases of acute hemiplegia occurring during epidemics of poliomyelitis and in the same family with children who developed typical spinal paralysis. Even more convincing are the cases of hemiplegia sometimes seen in which flaccid and spastic paralysis coexist. Müller,[90] Medin, Zappert,[91] Williams,[92] Neurath,[93] Calabrese,[94] Oppenheim,[95] Marie,[96] Wickman,[97] Parkes Weber,[98] Ash,[99] and Jones and Lovett [100]

83. Pasteur, W.: Tr. Clin. Soc. London **30**:143, 1896-1897.
84. Moebius: Schmidt's Jahrb. **204**:135, 1884.
85. Medin: Arch. de méd. d. enf. **1**:257, 1898.
86. Buccelli: Policlinico **4**:249, 1897.
87. Hoffmann: Deutsche Ztschr. f. Nervenh. **38**:146, 1909.
88. Schlesinger, in Verhandl. d. Gesellsch. deutsch. Nervenärzte, Wien, 1909.
89. Krause, P.: Deutsche med. Wchnschr. **35**:1822, 1909.
90. Müller, E.: München. med. Wchnschr. **56**:2460, 1909.
91. Zappert: Vers. d. ges. deutsch. Naturforsch. u. Aerzte, Königsberg, 1910.
92. Williams, E. C.: Lancet **2**:23 1899.
93. Neurath: Wien. med. Wchnschr. **59**:973, 1909.
94. Calabrese: Riforma med. **19**:29, 1903.
95. Oppenheim: Berl. klin. Wchnschr. **36**:405, 1899.
96. Marie, P.: Bull. et mém. Soc. méd. d. hôp. de Paris **35**:203, 1902.
97. Wickman: Acute Poliomyelitis, Nerv. & Ment. Dis. Monograph Series, 1913.

have published examples of this combination. Serologic evidence has been used also to support Strümpell's theory. Thus, Lovett refers to a case of hemiplegia in which the blood serum was found at the Rockefeller Institute to protect a monkey against a fatal dose of poliomyelitis virus. In another case of hemiplegia, George Draper believed he could make the diagnosis of Heine-Medin disease by the examination of the spinal fluid during the acute stage of the disease. Lovett has seen six cases of the hemiplegic type and believes that it is possible to identify them on clinical grounds. He gives the following description:

> The characteristic of the affection is that it is a mild hemiplegia presenting no different appearances from any other hemiplegia in its general spastic character—the position of the limbs, the awkwardness of the gait, and increase of reflexes—but it is mild and the characteristic point is that along with the spastic muscles one finds flaccid muscles irregularly distributed. In this way the type becomes a little irregular and unusual. In the cases observed there has been no mental deterioration and the progress of these cases under treatment by muscle training has been very much more rapid and satisfactory than in routine cerebral spastic paralysis.

It is necessary to point out that in some cases flaccid paralysis may be caused by a cerebral lesion and only atrophy can be accepted as proof that the spinal cord is involved. However, it must be admitted that the brain stem is frequently involved in poliomyelitis and that cranial nerve palsies are seen in a definite percentage of cases in most epidemics. In addition, two types of spastic weakness are sometimes seen; a spastic weakness of the legs, usually transient, associated with severe atrophic paralysis of the arms and a spastic weakness of one leg associated with a flaccid weakness of the opposite leg.

The anatomic support of Strümpell's theory is still meager. Foci of encephalitis are usually present in fatal cases of poliomyelitis, but these seem too small and too few to cause any paralysis. Harbitz and Scheel [101] have described the autopsies in two patients who developed cerebral symptoms during the Christiania epidemic of 1905. Neither of these patients, however, had hemiplegia. In one, a man, aged 38, there was an inflammatory process in the right temporal lobe, with softening of the cortex and similar areas on the mesial surfaces of both hemispheres. There were inflammatory changes in the basal ganglia, pons and medulla, and the cervical segments showed lesions which the authors considered typical of acute poliomyelitis. The second case was that of a child of 7 years. There was an acute inflammatory lesion in the left optic

98. Parkes Weber: Lancet **1**:591, 1889.

99. Ash, R. I.: Arch. Pediat. **42**:68, 1925.

100. Jones, Robert, and Lovett, R. W.: Orthopedic Surgery, New York, William Wood & Co., 1923.

101. Cited by Wickman (footnote 97).

thalamus, but no other change except for some hyperemia in the cervical cord. Rossi [102] and Lamy [103] have described lesions in two cases of mixed flaccid and spastic paralysis of long standing. They found changes in the spinal cord, similar to those that result from poliomyelitis, and also large scars in the cortex. Among forty autopsies performed in New York during the epidemic in 1916, there were congestion and edema of the brain in thirty-five. In one case of a young adult there was found intense congestion and softening of the central and parietal convolutions on one side with many small hemorrhages. In this case the Wassermann reaction was negative. It is of course difficult, if it is at all possible, to distinguish the inflammatory changes in the brain that are caused by the virus of poliomyelitis from those that are caused by some other acute inflammatory process, for example, epidemic encephalitis. Haüptli [104] and Hassin [105] have stated that the chief differences are in distribution and that the lesions are otherwise practically identical.

If one accepts the foregoing evidence to show that Heine-Medin disease may cause spastic paralysis of hemiplegic distribution, one must, nevertheless, admit that such cases are exceedingly rare. No examples of the hemiplegic type were seen in the great New York epidemics of 1907 [106] and 1911.[107] Wickman could not find any in the Swedish epidemic of 1906, although he personally examined many hundreds of patients. Only one case was noted in the Westphalian outbreak in 1909. Müller observed six cases in the Hesse-Nassau epidemic of 1909. Zappert reported five cases of infantile hemiplegia during the Austrian epidemic of 1908. Medin saw three in Stockholm during the epidemics of 1887 and 1895. In the Norwegian outbreak of 1905, Leegaard [108] discovered only two infantile hemiplegias among 848 cases of poliomyelitis. None were noted in the recent Detroit epidemic by Walker and McKenzie.[109] Almost as many cases of infantile hemiplegia must occur in these regions during an equal time interval when poliomyelitis is not prevalent. It is also noteworthy that in the experimental poliomyelitis of monkeys, in which the virus is injected directly into the brain, the chief lesions are found in the spinal cord and only

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102. Rossi: Nouv. iconog. de la Salpêtière **20**:122, 1907.

103. Lamy: Rev. neurol. **2**:301, 1894.

104. Haüptli, O.: Deutsche Ztschr. f. Nervenh. **71**:1, 1921.

105. Hassin, G. B.: Comparative Histopathology of Acute Anterior Poliomyelitis and Epidemic Encephalitis, Arch. Neurol. & Psychiat. **11**:28 (Feb.) 1924.

106. Sachs et al.: Epidemic Poliomyelitis. Report of Committee on New York Epidemic of 1907.

107. Peabody, Draper and Dochez: A Clinical Study of Acute Poliomyelitis, 1912 Monographs of the Rockefeller Institute.

108. Cited by Wickman (footnote 97).

109. Walker and McKenzie: Ann. Clin. Med. **4**:149, 1925.

atrophic paralysis develops. Batten,[110] who studied the subject carefully, stated that on clinical groups it seemed probable that about 10 per cent of all infantile hemiplegias are caused by the virus of poliomyelitis. This estimate seems excessive and it does not appear justifiable to attribute infantile hemiplegia to Heine-Medin disease except in the rare instances in which there is unequivocal evidence of involvement of the spinal gray matter in addition to the spastic hemiplegia.

RELATION TO EPIDEMIC ENCEPHALITIS

Since the appearance of epidemic encephalitis, numerous cases of the hemiplegic type have been reported. In many instances little if any evidence is offered to support the diagnosis, but it seems to be established that a hemiplegic type exists. Thus, Kennedy[111] described cases with apoplectic onset and papilledema, which he felt were probably related to epidemic encephalitis that was prevalent in New York when his observations were made, and Bramwell[112] has stated that an acute hemiplegia is sometimes the result of this cause. Buzzard and Greenfield[113] have published reports of cases of this nature with descriptions of the pathologic anatomy, and it is evident that one must consider epidemic encephalitis a possible cause of hemiplegia in young patients, even in infants. However, it must be noted that all the cases referred to in the foregoing occurred in adults in the fourth or fifth decade. Buzzard and Greenfield found large softenings in the cortex associated with severe infiltration and thrombosis of the cortical arteries and veins.

It does not seem probable that the infantile hemiplegias with which this paper deals can be related to epidemic encephalitis in many instances. The cases we are describing are not more frequent now that epidemic encephalitis is prevalent than they were some years ago when it was unknown. The infantile hemiplegias do not show the prolonged stupor that is a characteristic of the acute stage of encephalitis. The hemiplegic children do not exhibit the mental peculiarities that we have learned to consider characteristic sequelae of encephalitis. The hemiplegias tend to diminish; true epidemic encephalitis is often progressive. These hemiplegias usually show clinical signs of only one lesion and never the signs of a diffuse involvement of the brain. In addition, we have been unable to find any record of an acute infantile hemiplegia which at autopsy revealed lesions characteristic of epidemic encephalitis.

110. Batten, F. E., in Batten, Garrod and Thursfield: Diseases of Children, New York, Longmans, Green & Company, 1913.

111. Kennedy, Foster: Acute Benign Meningo-Encephalitis with Papilledema, Arch. Neurol. & Psychiat. **7**:53 (Jan.) 1922.

112. Bramwell, E.: Brit. M. J. **2**:649, 1921.

113. Buzzard, E. F., and Greenfield, J. G.: Brit. M. J. **2**:279, 1920; Brain **42**: 305, 1919.

RELATION TO MISCELLANEOUS INFECTIONS

Numerous observations have been made of the apparently close connection between various pyogenic infections and infantile hemiplegia. Thus, Marie, Thomas, Sachs and Peterson have noted the association between hemiplegia and tonsillitis. Heubner [114] has attributed a case to bronchitis, and Thomas and Gaudard [115] both observed cases of hemiplegia which followed the "croup" (diphtheria?). Fearnsides [116] believes that one of his cases resulted from otitis media. Numerous records of hemiplegia due to septic sinus thrombosis are to be found. Whipham [117] describes a case in which hemiplegia resulted from septic sinus thrombosis due to otitis media. Adson [118] has published the histories of two cases of hemiplegia which developed after mastoid operations. No autopsies were secured, but the author believed that the lesion was a local encephalitis which did not result in suppuration. Jeffreys [119] saw hemiplegia develop in a child who had been treated for pyelitis but who seemed well at the time of onset. An old *B. coli* infection was found in the kidney, and there were numerous evidences of invasion of the blood stream and embolic lesions in the brain and viscera. Southard and Keene [120] have reported several instances in which hemiplegia has resulted from infection of the blood stream with *Staphylococcus aureus*. In these cases multiple hemorrhages and thromboses with small foci of inflammation in relation to the blood vessels were found. Southard and Lucas [79] found, in their series of twelve cases of "infantile encephalitis," three cases associated with otitis media, two with pneumonia, one with peritonsillar abscess, and one with acute tonsillitis. Hahn [121] also has described a case of infantile hemiplegia, which occurred during an attack of erythema nodosum. Carretier [122] observed hemiplegia following a severe enteritis.

Congenital syphilis causes hemiplegia much less frequently than one would suppose. Lucas [123] found only one hemiplegia among sixty children with congenital syphilis, many of whom showed some evidence of involvement of the nervous system. Thomas, Osler, Sachs and Peterson attributed only seven cases in all to congenital syphilis.

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114. Heubner: Wien. med. Bl. **6**:373, 1883.
115. Gaudard: Contribution à l'étude de l'hémiplégie infantile, Geneve, 1884.
116. Fearnsides, E. G.: Brit. J. Child. Dis. **12**:136, 1915.
117. Whipham, T. R. C.: Brit. M. J. **1**:136, 1910.
118. Adson, A. W.; S. Clin. N. Amer. **4**:503, 1924.
119. Jeffreys, W. M.: Quart. J. Med. **4**:267, 1911.
120. Footnote 7 (second reference).
121. Hahn: Am. J. Obst. **71**:187, 1915.
122. Carretier: Arch. d. méd. d'enf. **17**:445, 1914.
123. Lucas, W. P.: Boston M. & S. J. **167**:278, 1912.

Seeligmüller [124] described a case of infantile hemiplegia with typical acute onset, which showed numerous cerebral tubercles at autopsy, a year later. He believed that tuberculosis must be a common cause of such palsies. Henoch [125] published the clinical history and anatomic observations in the case of a child with caseous pneumonia who suddenly developed hemiplegia. This was found to be the result of an embolus which had originated in the pulmonary vein. Cannata [126] and Herz [127] have also described hemiplegias in children who were suffering from tuberculosis.

RELATION TO CONVULSIONS. CONGENITAL VASCULAR ABNORMALITIES AND NONSEPTIC SINUS THROMBOSIS

Sachs [6] has stated that convulsions in infancy may cause cerebral hemorrhage and consequent hemiplegia. He describes a case in which hemiplegia occurred in an epileptic child after a severe seizure. An autopsy revealed a large, fresh hemorrhage over the surface of the hemisphere. Osler also believed that hemiplegia might result from a convulsion, and Thomas included a case in his series in which hemiplegia followed an epileptic attack. Spriggs and Higgs [128] presented a similar case in 1906, and Shore [129] has published another instance. It is well known that subconjunctival hemorrhages may follow an epileptic convulsion. Cases of this nature are excessively rare, however, and until one knows more about the anatomic observations one cannot be sure that the hemiplegia and the convulsion are not due to a common cause. Tumors of the brain and various types of congenital aneurysms may cause repeated convulsions and finally hemiplegia. Another cause of confusion is the transient palsy that may follow focal attacks. This is sometimes called an exhaustion palsy and is not caused by a gross lesion.

Osler [130] found a "congenital" aneurysm at autopsy in a child who died with a sudden hemiplegia. Cushing [131] and Cockayne [132] have both described hemiplegias in children who showed nevi on the face and hemangiomas involving the cortex. It may be mentioned at this point

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124. Seeligmüller: Jahrb. f. Kinderh. **13**:360, 1879.

125. Henoch, E.: Die atrophische Cerebrallähmung, Berlin, 1881, p. 236 (Vorlesungen über Kinderkrankheit).

126. Cannata, S.: Gaz. internaz. di. med. Chir., 1913, p. 31.

127. Herz: München. med. Wchnschr. **70**:238, 1923.

128. Spriggs and Higgs: Proc. Soc. for Study of Dis. Child., Nov. 16, 1906.

129. Shore, T. W.: Practitioner **34**:434, 1885.

130. Osler, William: Canada M. S. J. **14**:660, 1885-1886.

131. Cushing, Harvey: Cases of Spontaneous Intracranial Hemorrhage Associated with Trigeminal Nevi, J. A. M. A. **47**:178 (July 21) 1906.

132. Cockayne, E. A.: Proc. Roy. Soc. Med., Section of Diseases of Children, 1913.

that the nonseptic sinus thromboses which sometimes occur in various conditions associated with malnutrition and cachexia usually do not cause any localizing signs of a cerebral lesion and are often unsuspected during life. We have not been able to find any cases in which uncomplicated hemiplegia resulted from such a lesion.

MATERIAL FROM HARRIET LANE HOME

Nearly seventy cases of hemiplegia are contained among more than 50,000 case histories in the records from the Harriet Lane Home. Excluding those associated with heart disease, meningitis, tumor of the brain, birth injury,[133] and abscess, we find about thirty-eight which fall into the group under discussion. Five more infantile hemiplegias were added from the records of the medical department, which increased our material to forty-three. In sixteen of these, the hemiplegia followed immediately after some acute infectious disease (table 1). The etiology, therefore, is relatively clear. In seven cases the onset was associated with some local infection; pyelitis, otitis media, etc. Bacteremia was not demonstrated in any of these cases, and the connection between the infection and the cerebral lesion is, of course, open to doubt. Syphilis was the etiologic factor in only one case. In nineteen cases the children were considered healthy by the parents when the paralysis occurred (table 2). The past histories were analyzed to determine what importance previous infectious diseases might have. The histories, unfortunately, were not satisfactory in this respect, but previous infections did not seem to be especially frequent in these children.

The examinations of the spinal fluid are of considerable interest. If we except cases 16 and 17, in which there was contamination with blood, ten fluids were secured in the acute stage of the illness. In one there were 10 cells and a doubtful globulin reaction. The other nine fluids were normal in every respect.

Seven patients were subjected to operation. In six, old scars were found. In case 40, operation several weeks after the onset showed arterial thrombosis and cortical softening. Two autopsies were secured. In one, an old cyst was found which had probably resulted from a hemorrhage, and in the other, a fresh cortical softening. The latter, case 38, is given in greater detail. In all nine cases the lesions were in the cortex.

DETAILS OF CASE 34 FROM TABLE 1

Clinical History.—J. B., a white boy, aged 3 years and 11 months, brought into the Harriet Lane Home for Children in a state of coma, was the child of healthy parents. There were two siblings living and well; there had not been any miscarriages. Birth was normal and there was no evidence of birth injury. Growth

133. Ford, F. R.: Medicine **5**:121, 1926.

TABLE 1.—*Analysis of Twenty-Four Cases of Infantile Hemiplegia Following Acute Infections*

No.	Age at Onset	Preceding Infection	Signs and Symptoms	Spinal Fluid	End-result	Pathologic Anatomy
1	2 mo.	Pneumonia; otitis media	Sudden hemiplegias; no convulsions	.....	Residual hemiplegia	
2*	19 mo.	Pneumonia; lung abscess	Stupor; hemiplegia; hemianopia; no convulsions	Cells, 4; globulin, 0; negative Wassermann reaction	Residual hemiplegia	
3*	18 mo.	Pneumonia	Many convulsions on third day; hemiplegia	Cells, 1; globulin, 0; negative Wassermann reaction	Residual hemiplegia	
4*	9 mo.	Pneumonia; otitis media	Many convulsions month after onset; hemiplegia	Cells, 2; globulin, 0; negative Wassermann reaction	Residual hemiplegia	
5	2 yr.	Pneumonia; otitis media	Convulsions; left hemiplegia; loss of speech	.....	Hemiplegia; mental defect; epilepsy	S. 35517. Operation old softening in lower motor and frontal areas
6*	3 yr.	Measles	Convulsions; right hemiplegia; speech defect	.....	No paralysis; severe mental defect; petit mal	
7	7 mo.	Measles	Sudden hemiplegia in convalescence	.....	Epilepsy at 4 years.....	Path: 6378: Large cyst in cortex; atrophy and scarring of gyri
8	1 yr.	Measles	Convulsions; left hemiplegia	.....	Focal epilepsy at 2 years; no paralysis	
9	1½ yr.	Measles	Focal convulsions; right hemiplegia	.....	Great improvement in weakness month later	
10	3 yr.	Pertussis; pneumonia	Convulsions; right hemiplegia; loss of speech	.....	Epilepsy 6 months later; mental defect	S. 51510½, Operation: cortical atrophy and scarring
11	2 yr.	Pertussis	Sudden left hemiplegia few days after onset	.....	Focal epilepsy; hemiparesis	Operation: local atrophy and scarring of cortex
12	15 mo.	Typhoid fever....	Sudden convulsions; left hemiplegia	.....	Hemiplegia, mental defect; epilepsy at 7 years	
13	7 yr.	Typhoid fever.... otitis media	Convulsions; left hemiplegia	.....	Focal epilepsy; no mental defect	Operation: local cortical atrophy and scarring
14	4 yr.	Diphtheria	Focal convulsions; left hemiparesis	.....	Epilepsy; left hemiparesis	Operation: local atrophy of convolutions
15	1 yr.	Scarlet fever.....	Hemorrhages from mouth; sudden right hemiplegia; no convulsions	.....	Hemiplegia; mental defect; epilepsy began at 8 years	
16*	14 mo.	Bacillary dysentery	Focal convulsions; right hemiplegia	Altered blood in fluid.....	Residual hemiplegia	
17*	16 mo.	Congenital syphilis	Sudden convulsions; later hemiplegia; blood Wassermann reaction positive	Bloody fluid; positive Wassermann reaction	Death	
18	18 mo.	Pyelitis; temperature, 106	Sudden right hemiplegia; no convulsions	.....	Speech defective; mental defect; right leg weak	
19	9 mo.	Pyelitis	Convulsions; left hemiplegia	.....	Hemiplegia; epilepsy	
20*	2 yr.	Tonsillitis; temperature, 104	Vomiting; stupor; right hemiplegia; white blood cells 23,500	Cells, 10; glioulin, ±; negative Wassermann reaction	Death	
21*	17 mo.	Otitis media; high fever	Convulsions; left hemiplegia; hemianopia; white blood cells, 27,680	Cells, 4; globulin, 0; negative Wassermann reaction	Residual hemiplegia	
22	18 mo.	Otitis media.....	Fever three days; sudden left hemiplegia; no convulsions	.....	Residual hemiplegia	
23*	2 yr.	Otitis media.....	High fever one week; sudden focal convulsions; hemiplegia	Cells, 5; globulin, 0; negative Wassermann reaction	Recovery	
24	2 yr.	Diarrhea; temperature, 107	Convulsions; loss of speech, right hemiplegia	.....	No paralysis, slight mental defect, speech defect	

* Cases seen in the acute stage.

TABLE 2.—*Analysis of Nineteen Cases of Infantile Hemiplegia in Apparently Healthy Children*

No.	Age at Onset	Previous Infections	Signs and Symptoms	Spinal Fluid	End-result	Pathologic Anatomy
25	1 yr.	None	Convulsions, left hemiplegia, gradually disappearing	.....	Epilepsy; no weakness; no mental defect	
26	3 mo.	No past history..	Convulsions; right hemiplegia; improvement	.....	Epilepsy at 12 months; mental defect	Operation: atrophy and scarring of cortex
27	20 mo.	Varicella at 20 months	Fever one day; convulsions and hemiplegia next day	.....	Slight hemiplegia; some mental defect; loss of speech	
28*	5 mo.	None	Temperature, 107; drowsiness; convulsions; hemiplegia	Cells, 3; globulin, 0; negative Wassermann reaction	Epilepsy 2 months later; mental defect; hemiplegia	
29	2 yr.	Scurvy at 2 years, before previous infection ?	Fever one week; sudden convulsions; hemiplegia	.....	Epilepsy 2 years later; severe deterioration	
30	18 mo.	None	Fever; sudden coma; hemiplegia noted later	.....	Mental defect; residual hemiplegia	
31	10 mo.	Pneumonia at about 1 year, before previous infection ?	Fever one week; on second day convulsions; left hemiplegia	.....	Epilepsy; mental defect; residual hemiplegia	
32	3 yr.	Pertussis at 2 yr.	Sudden convulsions; hemiplegia	.....	Complete hemiplegia	
33	12 yr.	Measles, pertussis, malaria before previous infection	Sudden general convulsion; left hemiplegia	.....	Recovery	
34	3 yr.	No past history..	Sudden convulsions; hemiplegia; (poor history)	.....	Epilepsy; mental defect; residual hemiplegia	
35	10 mo.	No past history..	Sudden hemiplegia without convulsions	.....	Residual hemiplegia; epilepsy	
36*	5 yr.	Pertussis at 1 yr.	Vomiting; focal convulsions; right hemiplegia	Cells, 5; globulin, 0; negative Wassermann reaction	Recovery	
37	4 mo.	None	Sudden hemiplegia; convulsions	.....	Residual hemiplegia	
38*	3 yr.	Measles and scarlet fever before previous infection	Sudden convulsions; hemiplegia; coma; death	Cells, 2; globulin, 0; negative Wassermann reaction	Death	Path. 9033: cortical softening, thrombosis, bronchitis
39	18 mo.	Mumps, measles, varicella, pertussis	Convulsions; coma five days; left hemiplegia	.....	No weakness; slight mental defect; epilepsy	
40	2 yr.	None	Convulsions for months; sudden left hemiplegia	.....	Hemiplegia; mental defect; epilepsy	Operation: thrombosed vessels and softening in motor area
41	5 yr.	Measles at 2 yr.; malaria at 4 yr.	Convulsions, coma, right hemiplegia, weakness on left also	.....	Residual right hemiplegia, slight; no mental loss	
42*	10 mo.	None	Convulsions; fever; diarrhea; left hemiplegia	Cells, 6; globulin, 0; negative Wassermann reaction	No weakness; epilepsy	
43	3 yr.	Measles at 2 yr.; varicella at 2 yr.	Fever; right hemiplegia; no convulsions	.....	Recovery complete	

* Cases seen in the acute stage.

and development had been normal in every respect. At 6 months the patient had had measles, and a mild attack of scarlet fever occurred at 2 years. The general health had always been good. During the two weeks preceding entrance to the hospital, the patient had a slight cold in the head with a little nasal discharge. One day the child seemed irritable and would not eat breakfast. A few hours later, two severe generalized convulsions occurred, and the child remained unconscious after these seizures. The next morning he was still stuporous, and it was noted that the left arm and leg were limp. He was brought to the hospital twenty-four hours after the onset.

Physical Examination.—The patient was a well developed, well nourished boy, whose temperature was 100.5; pulse rate, 60; respiration, 20; weight, 38 pounds 11 ounces (17.5 Kg.). He was stuporous and restless. There was no rigidity of the neck. The ears were normal. The chest and abdomen were entirely normal, as were the throat and tonsils. The skin was clear, without eruption. The head and eyes deviated somewhat to the right, and the left arm and leg were limp and apparently paralyzed. The right plantar response was flexor; the left extensor. The tendon reflexes were about equal on the two sides; no clonus was elicited. The retinas appeared normal, and there was no suggestion of papilledema. The white blood cells numbered 10,600; hemoglobin was 75 per cent. Examination of the spinal fluid showed: cells, 2; globulin, 0; Wassermann reaction negative; mastic curve, 000000000000.

Course.—The temperature rose to 103, the coma deepened and the child died on the third day after the onset.

Pathologic Anatomy.—Autopsy was performed by Dr. Wiley Forbus. The brain was injected with a solution of formaldehyde through the carotid arteries before removal. When the skull was opened, the meninges appeared normal. The superficial veins of the pia-arachnoid were somewhat congested. The right hemisphere was swollen, and there was some herniation under the falx. On palpation the right frontoparietal cortex was soft and had not received the injection of solution of formaldehyde. Section revealed that the softening was confined to the cortex and that the basal ganglia and capsule were normal. There were no hemorrhages. The lesion was entirely confined to the distribution of the cortical branches of the right middle cerebral artery.

Microscopic sections showed merely necrosis of the softened areas and not any encephalitis. A premortem thrombus was found in the right middle cerebral artery just beyond the point where the penetrating branches to the base are given off. There was beginning organization, but inflammatory changes in the clot or vessel wall were not seen. All the cerebral arteries showed numerous thick intimal plaques composed of connective tissue with a good deal of fat in the interstices. This was mostly contained in phagocytes. Some plaques showed fine lamellae of elastic tissue. Every section of the cerebral arteries showed these intimal changes. In the right middle cerebral artery, there were numerous foci of necrosis in the media. The elastic lamellae were swollen and in some places entirely disintegrated, and the muscularis was reduced to half its thickness (fig. 1). The adventitia seemed normal. The other cerebral arteries showed less severe medial lesions, but well developed intimal plaques (fig. 2). Similar but much less severe changes were found in the arteries of the viscera and extremities. The venous sinuses were patent. The abdominal and thoracic viscera were normal. The heart was not enlarged, and the valves were smooth. There was some bronchitis which did not extend to the smaller bronchi. Infarcts or evidences of embolism were not found. Nothing to suggest syphilis or tuberculosis could be discovered.

Fig. 1.—Section through thrombus in the right middle cerebral artery. On the left the elastic tissue is destroyed and the muscularis is severely affected. The arrows point to broken down intimal plaques.

Fig. 2.—Section of right anterior cerebral artery, showing intimal plaque with reduplication of elastic lamellae. The slight medical changes are shown by the thinning beneath the plaque.

PATHOLOGIC ANATOMY OF INFANTILE HEMIPLEGIAS

HEMIPLEGIAS FOLLOWING ACUTE INFECTIOUS DISEASES

It is clear from the facts already detailed that the hemiplegias which follow the various acute infections in childhood depend almost invariably on arterial thrombosis, hemorrhage and embolism of the cerebral vessels. Many studies have been made of the vascular lesions which result from acute infectious diseases. One of the most extensive investigations is that of Wiesel,[134] who studied the blood vessels of 300 young patients who died of various infectious diseases including diphtheria, scarlet fever, pneumonia, typhoid fever and influenza. In many cases he found destructive changes in the smooth muscle and elastic tissue of the media, which sometimes resulted in necrosis. The intima showed elevated fatty plaques which were often grossly visible. These changes were focal, and other arteries, or even other segments of the same artery, might be unaffected. They did not reach a maximum until after the eighteenth day. Wiesel did not find any inflammatory phenomena. He ascribed these lesions to the bacterial toxin. The arteries most commonly and most severely involved were the cerebral, the coronaries and the aorta. Wiesel believed that these lesions healed within a few months. He found merely a few small scars in the muscularis when necropsy was performed a year or more after infectious diseases had occurred.

Scharpff [135] conducted similar studies and was inclined to emphasize the intimal proliferation. Frothingham [136] described essentially the same picture that Wiesel described. Klotz [137] believes he can distinguish two types of arterial lesions following acute infections: one, described in the foregoing paragraph, which is the result of the bacterial toxin; the other, a perivascular inflammatory process in the vasa vasorum, which he ascribes to the presence of the bacteria. Mallory [138] published excellent descriptions of both types of lesion in 1913. Recently, Brown [139] has reported careful studies of the aortic lesions after acute infections and has found inflammatory changes about the vasa vasorum which he believed were responsible for the necrosis in the media. Allbutt's [140] monograph contains numerous references to clinical observations of

134. Wiesel, J.: Ztschr. f. Heilk. **26**:107, 1905; **27**:262, 1906; Wien. klin. Wchnschr. **56**:15, 1906.

135. Scharpff: Frankfurt. Ztschr. f. Path. **2**:391, 1909

136. Frothingham, Channing: The Relation Between Acute Infectious Diseases and Arterial Lesions, Arch. Int. Med. **8**:153 (Aug.) 1911.

137. Klotz: Diseases of the Media, University of Pittsburgh Medical School publication, January, 1911.

138. Mallory, F. B.: Boston City Hospital Reports, 1913, p. 148.

139. Brown, M. H.: Ann. Clin. Med. **5**:353, 1926.

140. Allbutt, C.: Diseases of the Arteries, New York, The MacMillan Company, 1915.

thickening of the peripheral arteries in young people after severe infections.

To summarize, it is well established that after infectious diseases in childhood extensive vascular lesions may be found, which consist of fatty plaques in the intima that encroach on the lumen, and destructive changes in the media that weaken the arterial wall and tend to cause hemorrhages. Another possible factor in the production of vascular lesions is change in the coagulability of the blood. Rolleston states that in the hemorrhagic form of diphtheria the coagulation time is delayed. In other forms it is often diminished, hence the tendency to arterial thromboses and mural thrombi on the endocardium, which give rise to emboli. In hemorrhagic smallpox, in Rolleston's experience, there is also some disturbance in coagulation of blood as shown by a nonretractile clot. In anemia and chlorosis, it is stated that spontaneous thromboses may occur. In dysentery, the extreme desiccation and concentration of the blood may be of importance in favoring thrombosis. The claim of Gowers that infantile hemiplegia is commonly due to venous thrombosis is still unsupported by anatomic evidence, but venous thromboses are rarely studied and their results are largely unknown.

Although vascular accidents are in no sense to be considered specific effects of these diseases, the relative proportions of thrombosis, hemorrhage and embolism are different in different infections. In pertussis we found that cerebral hemorrhage is discovered in almost all cases in which persistent hemiplegia has developed, and it seems probable that the mechanical effect of the intense cerebral congestion that occurs during the paroxysms has a definite relation to this fact. Holt and Howland believe that the mechanical factor is most important, but Rolleston thinks that the cerebral lesions are the result of a toxic process. It is evident that embolism from the detachment of cardiac thrombi is the most frequent cause of the cerebral palsies that occur in diphtheria. This fact is easily correlated with the severe effect of the diphtheritic toxin on the heart. Only thromboses of the cerebral arteries have been found in the few cases of hemiplegia complicating typhoid fever that have come to autopsy.

We have already learned that in a small number of cases of the postinfectious hemiplegias of infancy, autopsy has revealed multiple hemorrhages and thromboses of the cerebral vessels. The term "hemorrhagic encephalitis" has been loosely applied to this condition. In some of these cases, for example that described by Toomey, Dembo and McConnell, the cerebral vessels show hyaline and degenerative changes without any inflammatory phenomena, and it seems clear that such lesions can be attributed only to the effects of the bacterial toxins. It is not at all clear why in some cases a single vascular lesion develops and in others multiple lesions occur, but it is probable that the process is the same and that the difference is merely in degree. Numerous

examples of "hemorrhagic encephalitis" show perivascular cellular accumulation and inflammatory changes in the vessels. The cases described by Southard and his co-workers and the case of Batten and Prickett may be referred to in this connection. Bacteria usually may be demonstrated in the tissues by appropriate stains, and the clinical picture is complicated by the evidences of invasion of the blood stream. Some secondary invader is generally to blame. "Hemorrhagic encephalitis" may follow almost any infectious disease, as Oppenheim and Cassirer [141] have shown, and indeed, a similar picture may be produced by carbon monoxide, hydrocyanic acid, arsphenamine and phosgene poisoning. It is evident that this condition cannot be considered a primary disease of the brain as Strümpell believed, but is merely the result of the action of various bacterial poisons on the cerebral vessels. Oppenheim and Cassirer believed that it is the commonest basis of infantile acquired hemiplegia, but Freud [142] is skeptical of this. Our results indicate that most cases of infantile hemiplegia depend on a single lesion.

Nothing is known of the cause of the transient palsies or of the cerebral palsies without demonstrable anatomic bases. Any discussion of these problems would be purely speculative.

A large number of observations on the morbid anatomy of long-standing infantile hemiplegias has been collected by Wallenberg, Osler, Freud, Sachs and Peterson, and it is clear that whatever the initial process may be, the end-results are local shrinking and scarring of the convolutions, the so-called circumscribed atrophic sclerosis, cavitation and the superficial shrunken patches, compared to wet-wash leather, which Cotard [143] termed "plaques jaunes." Little or nothing can be inferred about the primary process from such scars.

HEMIPLEGIAS IN APPARENTLY HEALTHY CHILDREN

Very few autopsies have been performed while the lesions were still fresh in cases of infantile hemiplegia that fall into this etiologically obscure group. Callender,[144] indeed, published reports of two cases in which cerebral hemorrhage occurred in children without apparent cause, but his descriptions are so meager as to be of little value. In 1888, Abercrombie described the case of a child who developed hemiplegia without any preceding illness. There was occlusion of the middle cerebral artery which the author believed was caused by embolism from some minute fibrinous vegetations on the valves of the heart. There had not been any symptoms of heart disease. Sachs found cerebral

141. Oppenheim and Cassirer: Die Encephalitis, Vienna, 1907.

142. Freud, S.: Die Infantile Cerebrallähmung, 1897; Nothnagel Spezielle Path. & Therap., vol. 9.

143. Cotard: Étude sur l'atrophie cérébral, Thesis, Paris, 1868.

144. Callender, G. W.: St. Bartholomew's Hosp. Rep. **5**:3, 1869.

hemorrhage in a case of hemiplegia which followed an epileptic seizure. A ruptured aneurysm was found by Osler in one case of infantile hemiplegia. He believed that there had been a congenital defect in the vessel wall. Talbot [145] has reported a case of hemiplegia in a healthy boy, aged 9. In a careful histologic study, he found intimal thickening in all the cerebral vessels with dilatation and rupture at one point in the middle cerebral artery. He could not find a cause for these changes and was inclined to attribute them to some unknown intoxication or infection. Hawthorne [146] observed hemorrhage into the left frontal lobe in a healthy boy, aged 14. He could not find any cause for this lesion. A right capsular hemorrhage in a girl, aged 10, was noted by Hugh Taylor,[147] and again postmortem examination did not reveal the cause. Bennett [148] refers to the case of a boy, aged 14, who suffered a hemorrhage into the basal ganglia. Quain [149] found hemorrhage into the right hemisphere in a child, aged 9 years. Sidney Phillips [150] found an unexplained pontile hemorrhage in a child, aged 14 months. Cerebral hemorrhage in a child of 1 year is reported by Conti [151] and a similar case of hemorrhage into the brain at the age of 2 months is described by Carpenter.[152] Potter and McGregor [153] describe an interesting case of pontile bleeding in a child of 4 years, who had been perfectly healthy previously. No changes in the cerebral vessels could be found, and a careful autopsy did not throw any light on the etiology. Ghetti [154] gives the history and anatomic observations in the case of a boy of 10 years who developed a right hemiplegia. A diffuse endarteritis was found in the cerebral arteries and a large hemorrhage into the internal capsule. The cause was obscure. Case 38 of our series also falls into this group of clinically obscure hemiplegias. Necropsy revealed a cortical softening which was the result of thrombosis of the middle cerebral artery. Some thickening of the intima of all the cerebral arteries was found.

Altogether, among sixteen autopsies, an unexplained change in the intima was found three times; embolism was reported once, and in twelve cases no abnormalities were found in the arteries and no cause

145. Talbot, F. B.: Contributions to Medical and Biological Research. Dedicated to Sir William Osler, 1919, p. 1004.

146. Hawthorne: Practitioner **109**:425, 1922.

147. Taylor, Hugh: Lancet **1**:291, 1905.

148. Bennett, J. H.: Principles and Practice of Medicine, p. 364, 1860.

149. Quain, quoted in Tanner and Meadows: Diseases of Infancy and Childhood, ed. 3, 1879, p. 166.

150. Phillips, Sidney: Lancet **1**:1680, 1909.

151. Conti, L.: Pediatria **29**:168, 1921.

152. Carpenter: Proc. Roy. Soc. Med. (Sec. Dis. Child.), 1909, p. 38.

153. Potter and McGregor: Edinburgh M. J. **32**:482, 1925.

154. Ghetti: Brit. M. J. **1**:1 (Epitome) 1910.

could be given for the hemorrhage. In the latter reports the clinical notes were meager and details of the histologic examinations were not given.

CONCLUSIONS

It seems possible to state definitely that the infantile hemiplegias that are associated with the acute infectious diseases are due to vascular lesions. Those which occur early in the course of the illness are, in the majority of cases, due to invasion of the blood stream by the primary organism or by some secondary invader. The palsies that develop during convalescence are the result of the vascular lesions in the cerebral arteries which Wiesel and others have described. These complications are common to all severe infections and are not in any sense specific, although apparently specific changes in the nervous system may be produced by variola, vaccinia, varicella, and perhaps by measles and mumps.

Final conclusions cannot yet be reached concerning the cause of the hemiplegias that occur in apparently healthy children. The obvious assumption of encephalitis is not supported by anatomic evidence. Only vascular lesions have been found in the few cases in which the fresh lesions have been studied. The vascular changes noted by Ghetti and Talbot and in case 38 of our series are similar to those which occur during infectious diseases and may possibly be related to the previous illnesses that these children had suffered. It is possible that invasion of the blood stream by pyogenic organisms from clinically latent foci of infection might be the cause of some instances of this nature. Congenital defects in the cerebral arteries might cause hemorrhage in some cases.

The present communication deals with only one phase of a large subject. Many cortical and brain stem syndromes, acute cerebellar ataxias and some cases of myelitis bear the same relation to the acute infectious diseases of childhood as the hemiplegias discussed. Dependable anatomic studies are still almost wholly lacking in these conditions.

THROMBOSIS OF THE CEREBELLAR AND VERTEBRAL ARTERIES ASSOCIATED WITH INTERMITTENT HICCUP

OBSERVATIONS IN A FATAL CASE *

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From a series of experiments reported previously,[1] I have found that a streptococcus having peculiar invasive power and other properties appears to be the cause of epidemic hiccup. Thus, spasms of the diaphragm sometimes associated with hiccup have been produced in animals by means of suspensions of nasopharyngeal swabbings containing the streptococcus, with pure cultures on isolation, and after many rapidly made subcultures, with filtrates of active cultures and with suspensions of the dead bacteria. This streptococcus, which has the peculiar property of inciting spasms of the diaphragm and other muscles, has been isolated during the attack from a series of cases of epidemic hiccup in different outbreaks, and has been proved absent from the throats of normal persons and in persons suffering from other diseases. It disappears from the throat as recovery ensues. It has been demonstrated in, and isolated from, the lesions in experimental animals, and the disease has been produced again on reinjection.

I shall report here the clinical, pathologic and experimental observations in the case of a patient who died of thrombosis of the posterior inferior cerebellar and vertebral arteries at a time when cases of hiccup were occurring in Rochester; in this case, intermittent hiccup was a prominent symptom.

REPORT OF A CASE

A man, aged 68, while he was a patient in the hospital undergoing preparation for prostatectomy, developed a moderate rise in temperature which lasted for four days after cystoscopic examination, Jan. 19, 1925. Following this, the temperature was normal for three days, and on January 27, from no apparent cause, pyrexia appeared. The temperature rose to 103.5 F. during the night (clinical chart). The patient was unable to talk above a whisper and manifested difficulty in swallowing. The next morning intermittent attacks of hiccup appeared, lasting for from five to ten minutes at a time. He vomited once and had several sinking spells in which he became extremely cyanotic and could scarcely breathe. On January 29, the hiccup (fig. 1), the difficulty in swallowing and the fever continued; the pulse became irregular, and general weakness became manifest. Later in the day the difficulty in swallowing, the

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* From the Division of Experimental Bacteriology, The Mayo Foundation.

1. Rosenow, E. C.: J. Infect. Dis. **32**:41, 1923; ibid. **32**:72, 1923; Diaphragmatic Spasms in Animals Produced with a Streptococcus from Epidemic Hiccup, J. A. M. A. **76**:1745 (June 18) 1921.

choking and syncopal attacks grew rapidly worse, paralysis of the right leg and arm ensued, and the patient died suddenly in one of these attacks, two days after the onset of symptoms.

Examination.—During the course of the disease the systolic blood pressure had been 142, the diastolic 80, the hemoglobin 75 per cent and the leukocytes 8,200; a blood Wassermann test had proved negative. There had been moderate pyorrhea; the tonsils were small, but contained cheesy plugs in the crypts. The right antrum and frontal sinuses had been cloudy, and nasal polyps were present. Examination by the Section on Neurology on January 29 revealed slight horizontal nystagmus, loss of the left corneal reflex, crossed anesthesia of the left side of the face and of the right side of the body, and symptoms of left vagohypoglossopharyngeal paralysis. The observations indicated lesions on the left side of the upper medulla, involving the nuclei of the ninth, tenth, eleventh and twelfth

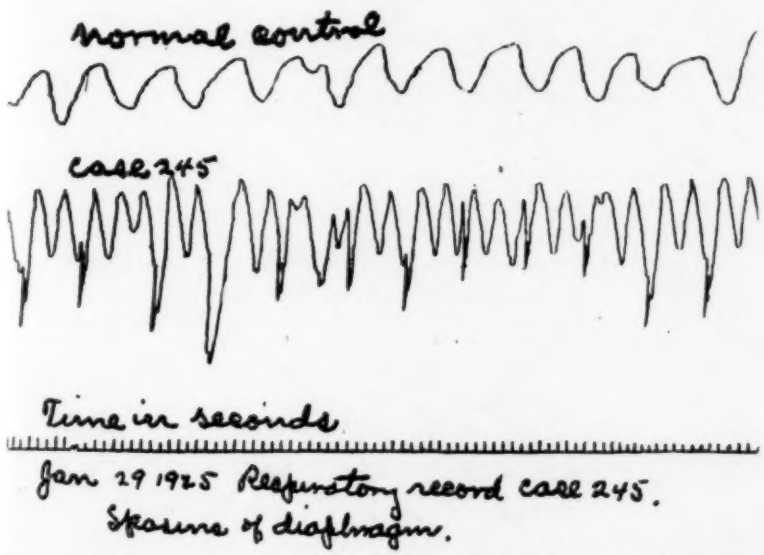

Fig. 1.—Respiratory record of the patient, January 29. Note the spasms of the diaphragm (indicated by the sharp, almost parallel lines) at the end of each second or third respiration, and the marked variation in time and amplitude of respiratory excursions in sharp contrast to that of a normal control person.

cranial and the spinal root of the fifth nerve. Encephalitis or thrombosis was considered as the most likely cause of the lesions in the medulla. Cultures were made from the blood and from the brain two hours after death, just before the body was embalmed.

Postmortem Examination.—Necropsy performed thirty-six hours after death revealed chronic sinusitis, nasal polyps, hypertrophy of the prostate with acute and chronic cystitis, ureteritis and pyelonephritis, multiple abscesses in the kidneys, edema of the lungs, marked arteriosclerosis, especially of the cerebral vessels, retrograde thrombosis of the left posterior inferior cerebellar and vertebral arteries, but no gross lesions of the brain and cord. The wall of the thrombosed vertebral artery was dilated at one point to constitute a small aneurysm.

Experiments.—Cultures and inoculations into animals were made from the nasopharynx and the urine during life and from emulsions of the brain and from

the blood aspirated from the heart and brachial vein after death. The swabbings from the nasopharynx on the morning of January 29 were suspended in 2 cc. of gelatin-Locke solution. From this suspension cultures and inoculations into animals were made in a manner previously reported. Two rabbits were inoculated intracerebrally, one receiving 0.1 cc., the other 0.2 cc. Both manifested tremors and twitchings of various muscles beginning in the masseters and spreading to the muscles of the ears, neck, shoulders and abdomen; coincidental with the appearance of spasms of the abdominal muscles, horizontal nystagmus, difficulty in breathing

Fig. 2.—Respiratory records of two rabbits (R740 and R 744) showing spasms of the diaphragm following injection of the streptoccocus from the nasopharynx and the blood respectively, and of a normal control rabbit.

and rhythmic spasms of the diaphragm occurred (fig. 2, R744). The spasms of the diaphragm in both animals appeared within twenty-four hours after injection and continued until death, twenty-four hours subsequently. This was apparently due to paralysis that began anteriorly, as did the spasms, and spread rapidly backward. At necropsy, marked congestion of the vessels of the meninges and edema over the anterior and posterior aspect of the medulla and cervical cord were found. The cerebrospinal fluid was slightly turbid. Cultures from the brain yielded a large number of colonies of the streptococcus; those from the blood gave no growth on blood-agar plates, but yielded the same streptococcus in glucose brain broth.

An attempt was made to isolate the characteristic streptococcus from single colonies on the surface of the blood-agar plates inoculated the previous day with the suspension of nasopharyngeal swabbings. Two rabbits received injections in the usual manner, with 0.1 and 0.2 cc., respectively, of the brain broth cultures in the fifth culture generation. Both animals remained free from symptoms.

Cultures from the blood of the patient, aspirated from the heart and brachial vein after death yielded a pure growth of a short-chained streptococcus. Two rabbits received injections, one with 0.1 cc., the other with 0.2 cc. of the primary cultures in hormone brain broth. The former manifested tremors and spasms of the masseters and muscles of the ears and neck and then recovered. The latter developed marked spasms of the diaphragm (fig. 2, R740) and other muscles, respiratory difficulty and paralysis of the fore extremities, and succumbed in twenty-four hours. Necropsy revealed marked congestion of the vessels of the meninges, a large hemorrhage at the base of the brain near the point of exit of the optic nerve and over the right lateral aspect of the medulla, and hemorrhagic edema over the anterior aspect of the medulla, upper cervical cord and surrounding cervical nerve roots. Cultures from the brain yielded countless numbers of streptococci; those from the blood, a few colonies. The emulsion of the brain made in salt solution, which yielded no growth in cultures, was injected intracerebrally into two rabbits (0.5 cc. each) and two monkeys (0.1 cc. each). All animals remained well and free from symptoms.

Cultures on blood-agar platings from the urine, obtained by catheter on the morning of January 29, yielded a large number of green-producing colonies of streptococci, together with a few colonies of *Bacillus coli*. The streptococcus from the urine in the fourth culture generation was injected into two rabbits, one receiving 0.1 cc. and the other 0.2 cc. of the hormone brain broth culture. One died during the night, and symptoms were not observed. Spasms of the diaphragm probably occurred, because hemorrhages were found in the diaphragm along the costal margin. The rabbit receiving the larger injection had evinced marked tremor and twitchings of the masseters and muscles of the ears, neck, abdomen, diaphragm and shoulders on the day after injection. The spasms lasted most of the day, but disappeared as ascending paralysis became manifest. The animal was found dead the second morning after injection. The observations at necropsy in both animals were similar to those following the injection of the strain from the nasopharynx and blood. The cultures from the brain and cord showed large numbers of streptococci, while the blood proved sterile.

The streptococcus which was isolated from the nasopharynx and from the urine of the patient during life and from the blood after death, and which produced spasms of the diaphragm or other muscles in animals, produced small, dry, nonadherent, rather flat colonies on horse blood agar, surrounded by a greenish halo; in glucose broth there was diffuse turbidity in twenty-four hours, which tended to become granular and to form sediment in forty-eight or seventy-two hours. Its size and form resembled the pneumococcus closely, but it produced chains of moderate length consisting of distinctly elongated diplococcus forms. A capsule was not demonstrable. The fermentative powers of the three strains were practically identical, acid being produced in dextrose, lactose, maltose, saccharose, raffinose and salicin. Inulin was not fermented, and all were bile-insoluble.

Microscopic Examination.—Sections were made at different levels of the cerebral cortex, pons, medulla and cervical, dorsal and lumbar cord of the patient. These were stained for lesions with hematoxylin and eosin and Nissl's method and for bacteria by a modified Gram's method. No noteworthy lesions or bacteria were found in sections of the cerebral cortex, pons and lower cervical, dorsal and

lumbar cord. Sections through different levels of the medulla and upper cervical cord revealed lesions, especially in two circumscribed areas on the left side, most marked at about the level of the nucleus of the vagus nerve. These areas, well illustrated in figure 3, stained poorly. The one in the posterior horn was wedge-shaped and measured approximately 9 by 3 mm. The other, in the anterior part of the medulla in the region of the olive, was round and measured about 4 mm. in diameter. Both lesions became rapidly less marked in sections taken from above and below this level. The main artery to both areas was completely plugged with a thrombus.

Most of the smaller vessels in the larger area were completely or partially filled with thrombi, whereas the smaller vessels in the smaller round area were empty. The thrombi contained a variable number of polymorphonuclear and round cells, and most of the plugged vessels were surrounded by edema, necrosis and poly-

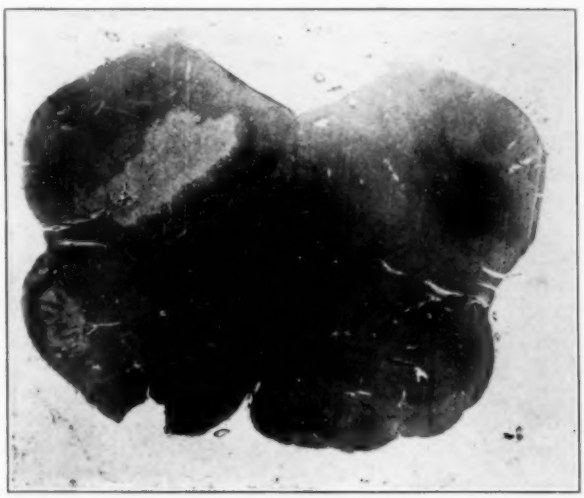

Fig. 3.—Section of the medulla of the patient. Note the poorly stained wedge-shaped area in the posterior horn and the poorly stained area in the region of the olive in the anterior quadrant on the left side. Hematoxylin and eosin, ×2.

morphonuclear infiltration (fig. 4). This was especially marked surrounding the large vessel entering the wedge-shaped area. Both areas revealed a varying degree of parenchymatous and perivascular infiltration. The latter was most marked, and the cells were chiefly polymorphonuclear in the areas showing parenchymatous leukocytic infiltration (fig. 5) immediately adjacent to the thrombosed vessels, whereas in the more remote parts the perivascular infiltration was chiefly lymphocytic. The parenchymatous cells in both areas stained poorly and irregularly. The nuclei were often fragmented. Nissl's granules were absent. Slight polymorphonuclear and round-cell infiltration of the pia over the left aspect of the medulla and upper cervical cord was also found. No microscopic lesions were found on the right side of the medulla and cervical cord. Prolonged search for bacteria revealed a moderate number of gram-positive diplococci, singly, in small groups or in chains of two diplococci within and adjacent to the lesions (fig. 6) in the medulla and in the infiltrated pia over the left aspect of the medulla and within the thrombus in one vessel.

Sections of the animals were made from different levels of the cerebrum, pons, medulla and cervical cord. The lesions were much alike in the animals inoculated with the streptococcus from the nasopharynx, the blood and the urine. In most instances there was an area of localized necrosis and leukocytic infiltration in the right frontal lobe at the point of inoculation; and there was leukocytic and

Fig. 4.—Thrombosed vessel surrounded by lymphocytes and polymorphonuclear leukocytes adjacent to the poorly stained area in the left posterior quadrant of the medulla. Hematoxylin and eosin, × 130.

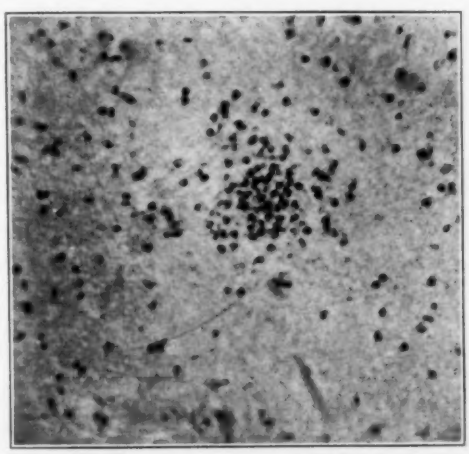

Fig. 5.—Area of necrosis and polymorphonuclear and round-cell infiltration in the poorly stained area in the region of the olive in the left anterior quadrant of the medulla. Hematoxylin and eosin, × 130.

round cell infiltration in the lateral ventricle surrounding the choroid plexus; in some instances this had extended to the central canal of the cord.

The tissues adjacent to the area of necrosis and leukocytic infiltration at the point of inoculation in the frontal lobe and those surrounding the lateral ventricle

and central canal revealed a variable degree of parenchymatous and perivascular infiltration, but this condition was most marked in the medulla. In the areas showing diffuse polymorphonuclear infiltration, the perivascular infiltration was also polymorphonuclear, whereas in the more remote parts, where little or no parenchymatous infiltration was found, the cells around the vessels, as in the

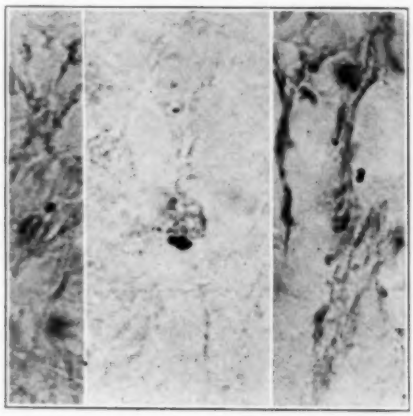

Fig. 6.—Diplococci in or adjacent to the poorly stained areas shown in figure 3. Gram, × 1000.

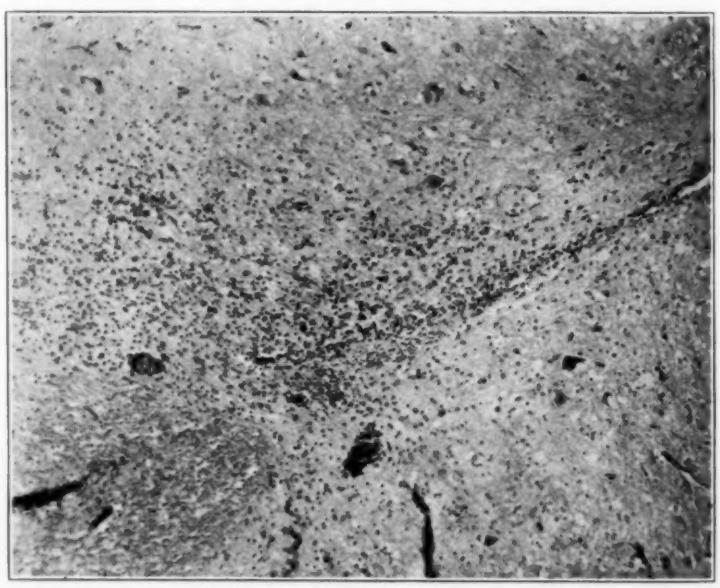

Fig. 7.—Thrombosis of vessels, cellular infiltration and perivascular and diffuse infiltration in the medulla of R 744 (fig. 2). Hematoxylin and eosin, × 50.

lesions in the medulla of the patient, were almost all lymphocytes or plasma cells. The meninges over the cerebral cortex showed only slight infiltration, chiefly by polymorphonuclears, in the sulci surrounding the vessels. This was especially marked over the anterior aspect of the medulla and cervical cord, and surrounding the sheaths of the roots of cervical nerves.

The lesions within the brain remote from the point of inoculation were few and consisted of small areas of necrosis with polymorphonuclear and round cell infiltration, chiefly in the cortex, whereas those in the medulla, while similar, were more numerous and more marked. In some instances the vessels were filled with thrombi (fig. 7).

Streptococci were readily demonstrable in the lesions in the rabbits that manifested spasms of the diaphragm and other muscles. They (fig. 8) were most numerous in the areas showing marked necrosis and in areas of infiltration within the substance, especially of the medulla and of the infiltrated meninges and sheaths surrounding the roots of the cervical nerves. There were few or no organisms to be found in the parts of the sections that were free from lesions, and in no instance were they found in the blood within the lumen of the vessels.

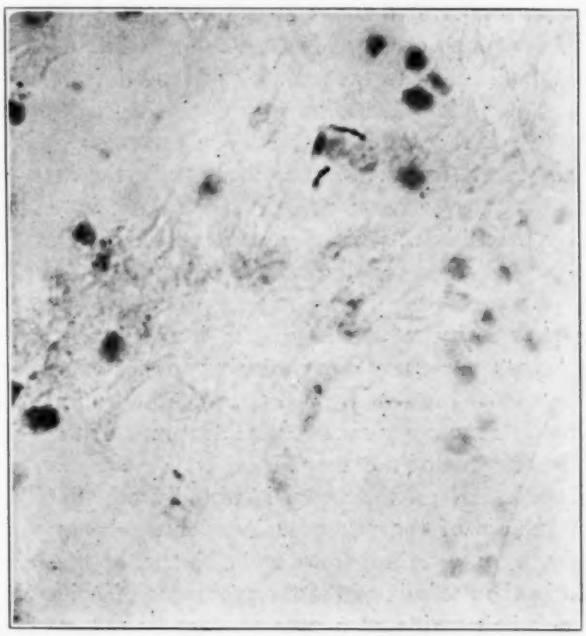

Fig. 8.—Diplococci of varying size, and streptococci in the area of infiltration in the medulla of R 744, shown in figure 7. Gram, × 1000.

COMMENT

The streptococcus isolated from the nasopharynx, the urine and the blood resembled in every respect the one which I have isolated in cases of epidemic hiccup. The lesions in the animals, while more widely distributed and more severe, were similar in type, including thrombosis, and (as regards maximal changes) in location to those found in the patient. In both instances, the infiltrating cells were chiefly polymorphonuclear in the areas where the lesions were most marked, and chiefly or wholly mononuclear in the perivascular spaces in the adjacent, more nearly normal tissues.

The symptoms referable to the medulla, even aside from spasms of the diaphragm of the patient and of most of the animals, were strikingly similar, and are adequately accounted for by the lesions which were found in the central nervous system, especially in the medulla and in the upper cervical cord. The causal relationship of the streptococcus to the lesions in the patient and in the animals is apparent through its demonstration in, or immediately adjacent to, the lesions, in thrombi and by negative cultures of the brain remote from the lesions in the medulla of the patient, and through the demonstration of its absence in normal tissues and vessels free from thrombosis. Thrombosis of the cerebellar and vertebral arteries appears to have been retrogressive and secondary to localization of the streptococcus in capillaries of the medulla, but it would probably not have occurred if the vessels had not become sclerotic and atheromatous incident to the patient's advanced age.

Other cases of prolonged hiccup were occurring in Rochester at the time the patient contracted his attack. The coincident high fever and the presence of the characteristic streptococcus in the infection atrium, in the blood in pure culture and in the urine in large numbers indicate clearly that this was not a case of simple thrombosis. Localization of the streptococcus in the kidney or urinary tract was favored, no doubt, by obstruction due to hypertrophy of the prostate. Streptococci having the power to incite spasms of the diaphragm practically never occur in the throats of persons except during attacks of epidemic hiccup. They have been proved absent from the throats in a number of cases of persistent hiccup due to other causes, such as tumor of the cerebellum or cerebrum and aneurysm of the aorta.

In consideration of all the facts, it would seem that this patient's attack of thrombosis of the posterior inferior cerebellar and vertebral arteries and death consequent thereto, and of intermittent hiccup was due to localization in the medulla of the streptococcus of epidemic singultus. Hence this may be considered a case of complicated epidemic hiccup. Even if it is granted that absolute proof of the exact relation of the streptococcus to the thrombosis is lacking, the observations at least emphasize the importance of searching for bacteria in the lesions in similar cases, especially if associated with hiccup.

EXPERIMENTAL MEDULLARY CONCUSSION OF THE SPINAL CORD IN RABBITS

HISTOLOGIC STUDY OF THE EARLY STAGES

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By concussion is meant the modification occurring in the spinal cord after a trauma has acted externally on the vertebrae without any direct lesion of the spinal tissue. Schmaus made the first experimental study of medullary concussion, by which he was able to establish the anatomic picture corresponding to indirect trauma of the spinal cord. Recently, during and after the World War, spinal concussion has been accurately investigated, and many papers have been published on this subject.

From the anatomic point of view, according to Rossi,[1] medullary concussion in man may be followed by: (*a*) intramedullary cavities; (*b*) the so-called primary traumatic necrosis of the nervous parenchyma; (*c*) large areas of medullary destruction; (*d*) hematomyelia.

Besides the action of a material agent, concussion may be the result of the so-called wind of explosion of French authors (Guillain[2] and Barré) in the first zone of action, or "zone of brisance" of English authors. Mairet and Durante[3] report medullary concussion due to the vibration of the air following high explosions.

Authors who have studied spinal concussion experimentally have used different methods to produce it. Some of them directly struck the spinal region; others, among them Schmaus[4] himself, have interposed a wood plank between the vertebral column and the percussion instrument; others, Schterbach,[5] have made use of a special vibrating apparatus, and others, D'Abundo[6] and Ingvar, have provoked the concussion by means of repeated centrifugalization of small animals.

The lesions found by Schmaus[4] in rabbits and guinea-pigs can be summarized as follows: swelling of the axis cylinder, its fragmentation and, in the most severe lesions, its granular degeneration. In a transverse

1. Rossi, O.: Osservasioni neurologiche sulle lesioni del sistema nervoso da traumi di guerra, Tipografia Sassarese, 1921.

2. Guillain, G.: Trauvaux neurologiques de guerre, Paris, Masson et Cie, 1921.

3. Mairet et Durante: Études experimentales des lésions commotionelles, Rev. neurol. **35**:97, 110 and 228, 1918.

4. Schmaus, H.: Vorlesungen über die pathologische Anatomie des Rueckenmarks, Wiesbaden, J. Bergmann, 1901.

5. Schterbach, H.: Des alterations de la moelle épinière chez le lapin sous l'influence de la vibration intensive, Encéphale V. **2**:521, 1907.

6. D'Abundo, G.: Alterazioni del sistema nervoso centrale consecutive a particolari commozioni traumatiche, Riv. ital. di neuropat. **9**:145, 1916.

section the axis cylinder appears enlarged, forming the so-called hyaline bodies. The nerve cells show a more or less pronounced chromatolysis and degeneration. The ependymal canal, dilated, here and there shows deformation and broken outlines. The degenerative changes of the white matter are more pronounced along the peripheral zone of the spinal cord, which shows dilated myelin sheaths and degenerated axis cylinders. The lesions correspond to the "Randdegeneration" of German authors. The neuroglia cells are here and there enlarged. In more severe cases, localized areas of necrosis are seen, and in the extremely severe cases, defined cavities are encountered, especially in the posterior columns.

The histologic observations of Schmaus were later confirmed by Chipault (1893), Alessi (1896) and Lepine (1900). One of the most accurate investigations on the subject is the work of A. Jakob [7] (1919). In addition to the lesions mentioned, in 1921, L. Cornil [8] was able to confirm the lesions of the posterior roots which Jakob had already described. Other authors have paid special attention only to some of the histologic components of the pathologic lesions. In this line of research, Lutzemberger (1897) claimed that the chief lesion of the nerve cell was dislocation of the chromatin bodies toward the pole of the cell, while Kirchgässer [9] believed that rarefaction and occasionally complete disappearance of the Nissl bodies was the most characteristic change. The nucleus, according to this author, apparently does not suffer, while the nucleolus is shrunken and somewhat deformed.

Parascandalo, Gudden, Scagliosi (1898) and Marinesco (1909) have found more or less the same type of lesions in the nerve cells: swelling of the body, chromatolysis, vacuolization and homogenization of the nucleus. A special modification of the neurofibrillar reticulum of the cells has been found by Todde,[10] using the Donaggio method for neurofibrils. The lesions consist in a condensation of the endocellular reticulum which is noticeable as early as one and one-half hours after the trauma. The external form of the nerve cells has been found modified by De Lisi,[11] who describes, besides breaking down of the Nissl bodies, a certain displacement of the nucleus. This author found the endocellular reticulum intact.

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7. Jakob, A.: Zur Pathologie der Rückenmarkserschütterung, Ztschr. f. d. ges. Neurol. u. Psychiat. **51**:297, 1919.

8. Cornil, L.: Étude anatomo-pathologique de la commotion médullaire, Thèse de Paris, 1921.

9. Kirchgässer, G.: Experimentelle Untersuchungen ueber Rückenmarkserschütterung, Deutsche Ztschr. f. Nervenh. **2**:400, 1897.

10. Todde, G.: Richerche sulle alterazioni del reticolo neuro-fibrillare endocellulare da trauma sperimentale, Riv. Sper. di freniat. **33**:751, 1907.

11. De Lisi, L.: Richerche sperimentali sulle alterazioni nervose centrali degli animali sottoposti a commozione cerebrale, Riv. Sper. di freniat. **41**:249, 1915.

Small areas of necrosis of the gray matter have been described by Schterbach, who found also cellular lesions of the afore mentioned type, although the neuroglia reaction was poor. Some areas of more or less extensive necrosis have been found by D'Abundo [6] after repeated centrifugalization of small animals. The necrosis was more localized in the posterior columns where the elementary histologic lesions were represented by swelling of the axis cylinder, fragmentation, degeneration of the myelin sheath and minute focal hemorrhages. Sven Ingvar, using the same procedure, found that the nucleolus was displaced toward the periphery of the nucleus.

A few authors, however, as Cavicchia and Rosa, deny any organic substratum to the medullary concussion. Their reports are, however, liable to criticism as the lesions found in their cases were attributed by the authors to the restlessness of the animals following the trauma rather than to the trauma itself.

Besides the experimental studies of spinal concussion, an important contribution to the knowledge of the pathology of this lesion has been given by the study of war lesions. This contribution followed the earlier papers of Obersteiner (1879), Dumenil and Petel [12] (1885), Schmaus (1890), Johnson, Smith and Watts (1896-1897), Minor, Lax and Müller [13] (1898), Lloyd, Hartmann [14] (1900), Löhrisch, Petren, Spiller [15] (1903), Sencert (1905), Warrington,[16] and Laquer and Vogt [17] (1911).

Recent investigators of this subject are: Jacobsohn, Trommer,[18] Nonne, Reinhardt, Jakob, Spatz,[19] Borst, and Marburg [20] in Germany; in France: Claude and Lhermitte,[21] Roussy, d'Oelsnitz, Ecot, Villandre,

12. Dumenil and Petel: Pathologie nerveuse, Arch. de neurol. **9**:149, 1885.

13. Lax and Müller, L.: Ein Beitrag zur Pathologie und pathologischen Anatomie der traumatischen Rückenmarkserkrankungen, Deutsche Ztschr. f. Nervenh. **12**:333, 1898.

14. Hartmann: Klinische und pathologisch-anatomische Untersuchungen ueber die unkomplizierten, traumatische Rueckenmarkserkrankungen, Jahrb. f. Psychiat. **19**:380, 1900.

15. Spiller, W. G.: Traumatic Lesions of the Spinal Cord Without Fracture of the Vertebrae, University of Pennsylvania, M. Bull. **15**:483, 1903.

16. Warrington: Concussion of the Cord: Commotio Spinalis, Rev. Neurol. & Psychiat. **8**:271, 1910.

17. Laquer and Vogt: Beitrag. zur Klinik und Anatomie der traumatischen Haematomyelie, Monatschr. f. Psychiat. u. Nervenh. **29**:35, 1915.

18. Trommer: Lokale Haematomyelie, Neurol. Centralbl. **34**:617, 1915.

19. Spatz, H.: Ueber degenerative und operatorische Vorgänge nach experimentellen Verletzungen des Rückenmarks, Ztschr. f. d. ges. Neurol. u. Psychiat. **58**:327, 1920.

20. Marburg: Pathologische Anatomie und Klinik der traumatischen Schädigungen des Rückenmarks, Deutsche Ztschr. f. Nervenh. **70**:10, 1921.

21. Claude and Lhermitte: Étude clinique et anatomo-pathologique de la commotion médullaire directe par projectiles de guerre, Am. de méd. **11**:479, 1915.

Cornil,[8] Delattre, Souques and Demolle,[22] and Mlle. Francais; in the United States: Frazier,[23] Hassin,[24] Mussen,[25] A. Reginald Allen, Solomon and Neister. In Italy the problem has been studied from the clinical point of view by d'Abundo, Sala and Bonola, and from the pathologic point of view by Rossi and later by Ferraro.[26]

METHOD EMPLOYED

The object of this article is to supplement my previous paper [26] on the histology of medullary concussion in which the lesions seen ten days after the trauma were the earliest stages described. Here I shall complete the reports for the experimental method by recording the histology of the very early stages of concussion.

For this purpose I have used rabbits in which I caused concussion by hitting them on the vertebral region with an iron rod. I have taken care to use rabbits of almost the same size, hitting them with approximately equal force. No anesthetic was used. For the purposes of this investigation only those rabbits were used which survived and appeared healthy from the time of concussion until they were killed, at different intervals of time after the trauma.

REPORT OF OBSERVATIONS

RABBIT 1.—Concussion was produced in the dorsolumbar region. The animal was killed one hour after the trauma.

HISTOLOGIC EXAMINATION

Lumbar Region.—General Aspect: In the white matter no cavities, hemorrhages or areas of necrosis were detected. The gray matter appeared grossly normal. The ependymal canal was dilated but not extremely, and dilatation of the perivascular spaces was noticed in the vicinity of the central canal.

Detailed Examination: The sulcus medianus anterior was dilated, and on each of its sides the medullary tissue appeared loose in texture. The axis cylinders appeared rather deeply stained, enlarged and deformed, surrounded by a swollen myelin sheath. The interstitial connective network did not show appreciable changes, although occasionally here and there the neuroglia cells were slightly enlarged in both the bodies and the prolongations. Nowhere in the section did the

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22. Souques and Demolle: Rammolissement de la moelle épinière par contusion, Rev. neurol. **29**:101, 1916.

23. Frazier, C. H., and Allen, A. R.: Surgery of the Spinal Cord, New York, D. Appleton Company, 1921.

24. Hassin, G. B.: Histopathologic Changes in Spinal Contusion, Arch. Neurol. & Psychiat. **13**:369 (March) 1925.

25. Mussen, Aubrey: The Finer Histological Changes in the Traumatic Degeneration of the Spinal Cord, Rev. Neurol. & Psychiat. **14**:417, 1916.

26. Ferraro, A.: Contributo alla conoscenza dell'anatomia patologica della distruzione primitiva del midollo spinale (cosi detta "Necrosi traumatica") Il Cervello Anno **1**:361, 1922. Complete references to the bibliography of this subject will be found in this article.

osmic acid of the fixative fluid (Flemming) appear to be reduced. The density of the inner layers of the tissue contrasted with the looseness of the peripheral areas, as seen in figure 1.

In the lateral columns the axis cylinders were diffusely enlarged but did not form a localized area as in the anterior column. Along the peripheral zone of the section the neuroglia reaction appeared more pronounced. The sulcus medianus posterior was not dilated and the medullary parenchyma close to the sulcus was normally dense in structure. Adjacent to well preserved areas, an area was seen in which the parenchyma was more or less damaged, axis cylinders showing

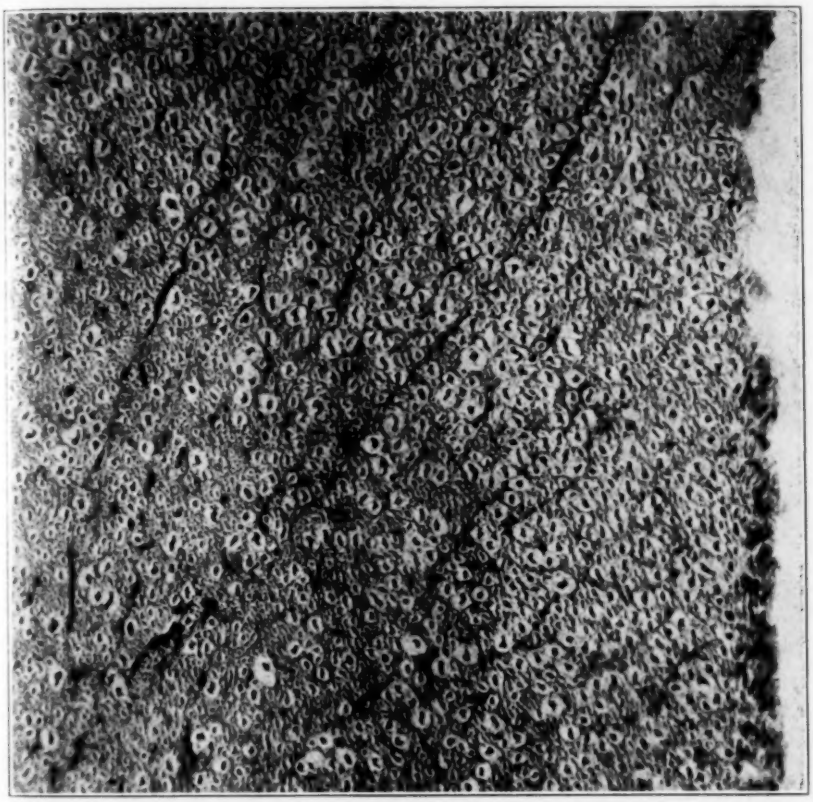

Fig. 1.—One hour and a half after the trauma; swelling of the axis cylinders. The difference between the external layers of the section bordering the sulcus medianus anterior and the internal layers is distinct. Mallory stain: aniline blue and orange G.

the same aspect already described in the interior column. The separation between the damaged and the preserved area was rather sharp.

In the gray matter, occasional, very minute foci of necrosis were seen. Surrounding some of the small blood vessels a few red blood cells were extravasated. The nerve cells were deeply stained and the chromatin bodies appeared to be condensed either along the periphery of the cell body or surrounding the centrally located nucleus. The neurofibrils showed the peculiar aspect described by Donaggio as conglutination of the neurofibrils; the endocellular reticulum no

longer appeared fibrillar but condensed, the condensation being found at times along the periphery of the cell body and at times surrounding the central region.

The nucleus of the nerve cells as a rule occupied the central region of the body, and no deformations were seen. The nucleolus of some cells was dislocated along the nuclear periphery, but no nucleolus was detected in the cytoplasm. Blood vessels appeared normal, and practically no changes of their walls were noticed.

Above and below the region of concussion the lesions decreased in intensity with the distance from the area of percussion. The axis cylinders were less involved, the perivascular spaces were less dilated and the nerve cells better preserved.

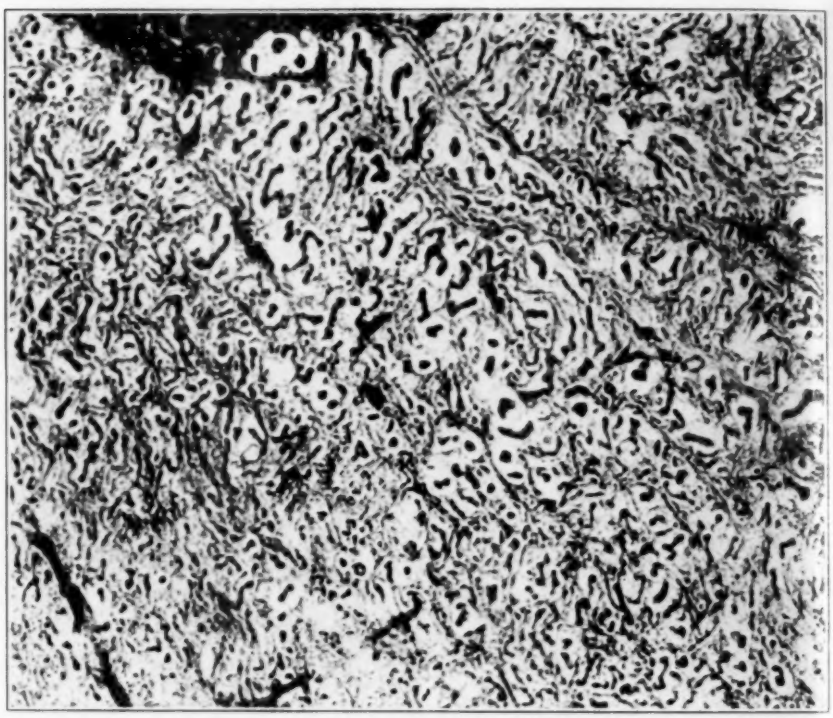

Fig. 2.—Four hours after the trauma; zone of entrance of the posterior root; swelling, deformity and fragmentation of the axis cylinders. Mallory stain: aniline blue and orange G.

Rabbit 2.—Concussion was produced in the lower dorsal region. The animal was killed four hours later.

Histologic Examination.—The lesions resembled closely those already described one and one-half hours after the concussion. The meninges were normal. There were no areas of hemorrhage. The central ependymal canal was dilated and the ependymal cells showed evident enlargement of the cytoplasm. The myelin sheaths were swollen to the extent described, but osmic reduction was not yet detected, except in a few small spots. The axis cylinders were enlarged and deformed. The neuroglia cells were, however, hypertrophic, showing here and there an enlarged body and enlarged prolongations. In the gray matter a few nerve cells

showed an eccentric nucleolus, and in one of the cells the nucleolus was seen on its way out of the nucleus, half way into the cytoplasm. The nerve cells were somewhat round, and the Nissl bodies were condensed. Another peculiarity was the presence of broken lines crossing the cell body; at times the cells showed only broken outlines and no involvement of the cytoplasm. The prolongations of the cells appeared swollen and some of them were fragmented. The fragmentation line was irregular and sometimes filled with fine granular material. Practically no nerve cells showed signs of secondary reaction. The zone of entrance of the posterior roots showed deformity of the axis cylinders, sometimes fragmentation and swelling of the myelin sheaths, as seen in figure 2.

Rabbit 3.—The trauma was inflicted at the dorsolumbar level. The animal was killed twelve hours after the concussion.

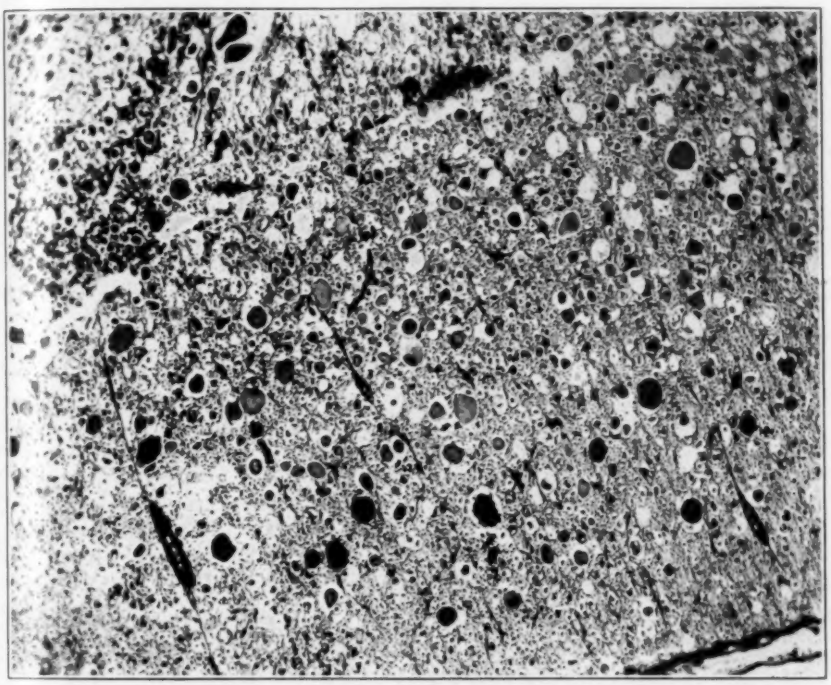

Fig. 3.—Twelve hours after the trauma; deformity and enlargement of the axis cylinders as seen in cross section (bodies of Schmaus or bolas of Cajal). Fixation in Flemming fluid, Mallory stain.

Histologic Examination.—The meninges showed a peculiar aspect at this period due to relaxation of the connective tissue, which gives the impression of a certain amount of thickening. The gray matter showed several areas of necrosis the outlines of which were irregular. The central canal was displaced, deformed and broken and was lined by hypertrophic ependymal cells. Occasionally, minute foci of red blood cells were encountered. The white matter was the seat of a highly degenerative process. The lesions were prominent in the anterior and lateral columns. For the first time osmic reduction was seen. The reduction took place in the myelin sheaths and appeared variably diffuse. In fact, some of the myelin sheaths showed only a few black spots while others showed a larger

involvement. Others still showed diffuse circular reduction of the osmic so that the axis cylinders appeared surrounded by black rings. At times the ring was narrow; at others it appeared thick. Occasionally the osmic reduction overlapped into the axis cylinder so that the transverse section of the nerve fiber appeared as a round black spot, the center of which was lighter than the periphery.

The osmic degeneration did not represent the only type of lesion, as the histology of the concussion was still characterized by primary involvement of the axis cylinder itself. This type of lesion seemed to be independent of the osmic degeneration of the myelin sheath. In these cases the myelin sheath appeared to be only more or less swollen and somewhat loose in texture while the axis cylinder was more or less enlarged and deformed. The structure of the axis cylinder was sometimes granular and occasionally was deeply stained. The enlargement of the axis cylinder represented the earlier stage of the primary fiber reaction while the more advanced process was represented by greater degeneration and by eventual resorption of the nerve fiber. The volume assumed by the enlarged axis cylinder varied from one to another as seen in figure 3. The neuroglia cells were markedly enlarged, the protoplasm and the prolongation being evidently hypertrophic. The changes involved the fixed neuroglia cells of the reticulum. No free neuroglia cells were seen, nor were special inclusions detected in these cells. The greatest reaction was present inside and surrounding the necrotic foci, but the reaction was also definite where the white matter appeared more or less well preserved. The blood vessels showed apparent thickening of their walls, the process being presumably much more of the relaxation type (Lockerung of German authors). There was as yet no participation of the mesodermal tissue in the pathologic process; the blood vessel walls showed no hypertrophy or migration of their cellular elements. The nerve cells were deformed, being frequently round with more or less condensed Nissl bodies, a few even showing swelling of the bodies with displaced nuclei.

At this stage the spinal roots of the region of concussion showed typical degenerative changes which could not be considered secondary to the lesion of the nerve cells. The radicular lesions were found in both anterior and posterior roots, but especially in the latter, while no lesions were detected in the spinal ganglia. The lesions of the axis cylinder resembled in type the lesions already described for the columnar fibers and were present in both the spinal root and the radicular zone of entrance. In this region the swelling of the axis cylinders, as well as its deformity, was evident. Some of them ended with the special enlargement known as Schmaus bodies or bolas of Cajal. A few axis cylinders were fragmented. In cross-section of the nerve roots the axis cylinder appeared enlarged, variably deformed and surrounded by a swollen myelin sheath. No osmic acid reduction was noticed.

The lesions above and below the region of concussion extended for two or three segments and were microscopically noticeable. The intensity of the lesions decreased with the distance from the traumatic zone. The main lesions in the less involved segments were represented by a peripheral zone of degeneration involving especially the myelin sheaths, which showed a moderate degree of osmic reduction. The axis cylinders were slightly enlarged and deformed. The gray matter appeared well preserved and the central canal filled with exfoliated ependymal cells. The nerve cells were slightly deformed, but no severe changes were detected. Occasionally the nucleolus occupied an eccentric position. The neuroglia cells were diffusely enlarged, but no migratory cells were seen. Both the anterior and the posterior sulci appeared normal. The posterior roots showed moderate degenerative changes of the type already described.

RABBIT 4.—The animal was killed eighteen hours after concussion.

Histologic Examination.—The lesions were severe at the level of the trauma where the section appeared loose in texture, the reticular connective framework being broken down. Several small empty areas were seen where the axis cylinders were no more detected. The gray matter was severely damaged, and the central canal appeared with broken outlines as if from an explosion. Surrounding the gray matter, the lesions of the white matter were pronounced and the whole

Fig. 4.—Eighteen hours after the trauma; lesions of the axis cylinders surrounding the gray matter. The internal layers of the lateral column are much more damaged than the external; Mallory stain.

picture contrasted with the other cases; the lesions here were more severe in the central region than in the periphery. Figure 4 shows the axis cylinders greatly deformed along the central gray matter while the peripheral zone is better preserved. Small areas of hemorrhage were present in the gray matter but none in the white matter. The detailed examination showed that the degenerative lesions were of the same type as the one already described in the earlier stages.

Here the presence of empty meshes was somewhat pronounced, the degenerative stage of the axis cylinder being more advanced. The nerve fibers were markedly enlarged and deformed, some of them showing a granular aspect while a few others were deeply stained. The prevailing type of degeneration was of the albuminous type involving the axis cylinder, while the myelin sheaths showed limited osmic acid degeneration.

The reaction of the neuroglia cells was still limited to the fixed elements of the reticulum ("Fixabraümzellen"). Only occasionally a neuroglia cell was seen free of connections in an area of disintegration. The fixed neuroglia cells with enlarged body and prolongations and the neuroglia cells showing a somewhat degenerated nucleus belong to the category of cells that Jakob has denominated "myeloclasts" or "myelophages" which, according to his views, elaborate in situ the disintegrated waste products before transmitting them to the mobile ectodermic cells or to the mesodermic "Abraümzellen." With the Scharlach R method, the gitter cells (fixed abraüm cells) show the presence of granular waste products in the stage of transformation into neutral fat (brilliant red color). The blood vessels showed moderate relaxation of their walls, but no hyperactivity of their cellular elements. The nerve cells were slightly deformed, many of them being deeply stained while others showed a minute fragmentation of the Nissl bodies. A few of them showed the signs of traumatic lesions already described in the earlier stages: more or less severely broken outline, eccentricity of the nucleolus and occasionally its displacement in the cytoplasm, fragmentation and degeneration of the cell prolongations.

Above and below the traumatic zone there was dilation of the anterior as well as of the posterior sulcus and of the central canal. No focal lesions, however, disturbed the gross architecture of the spinal cord. A degenerative process, of moderate degree, was pronounced along the peripheral zone. The myelin sheaths showed a moderate degree of osmic acid reduction, while the axis cylinders were better preserved, being only slightly enlarged and deformed. The degenerative process in some of the nerve fibers was evidently independent of the degeneration of the myelin sheath. No special inclusions were detected in the enlarged neuroglia cells. No areas of hemorrhage were encountered. A few cells showed swelling of the body and dislocation of the nucleus. Blood vessels showed apparently thickened walls. The ependymal lining cells were enlarged, and the subependymal glia tissue showed a moderate reaction of the protoplasmic type.

Rabbit 5.—Concussion was caused by the usual method and the animal was killed thirty hours later.

Histologic Examination.—The main picture corresponding to this stage was represented by a marked peripheral degeneration (Randdegeneration) which in this case had reached a considerable degree, involving both the myelin sheaths and the axis cylinders. Large empty spaces, previously occupied by the nerve fibers, were encountered. The myelin sheaths were the seat of intense osmic acid reduction, while the enlarged and deformed axis cylinders were few compared with earlier stages (fig. 5). The degeneration was more advanced at this period, and some of the nerve fibers showed a granular aspect associated with poor staining properties. Some of the neuroglia cells, the body and prolongations of which were enlarged, more or less completely surrounded the axis cylinders. Other cells were seen free in the necrotic areas, occasionally assuming an ameboid form. Here and there a neuroglia cell showed small osmic acid inclusions. The neuroglia reaction surrounding the central canal, which was considerably distorted and broken, was definite. The nerve cells did not show any appreciable changes from the earlier type of lesions.

The spinal ganglion cells appeared normal, while the radicular zone of the posterior roots was badly damaged.

RABBIT 6.—The animal was killed forty-five hours after the concussion.

Histologic Examination.—There was no appreciable change from the type of lesion described in the stage of thirty hours after the concussion. The degeneration still predominated in the ectodermic tissue, cells of the blood vessels still being inactive. The degeneration was scattered throughout the white matter, and the osmic reduction prevailed along the peripheral zone.

RABBIT 7.—The animal was killed seventy hours after the concussion.

Histologic Examination.—The neuroglia reaction at this time was more pronounced, and the body cell was greatly enlarged. The prolongations were thickened, and occasionally the cell assumed the type of the "Monstergliazellen" with

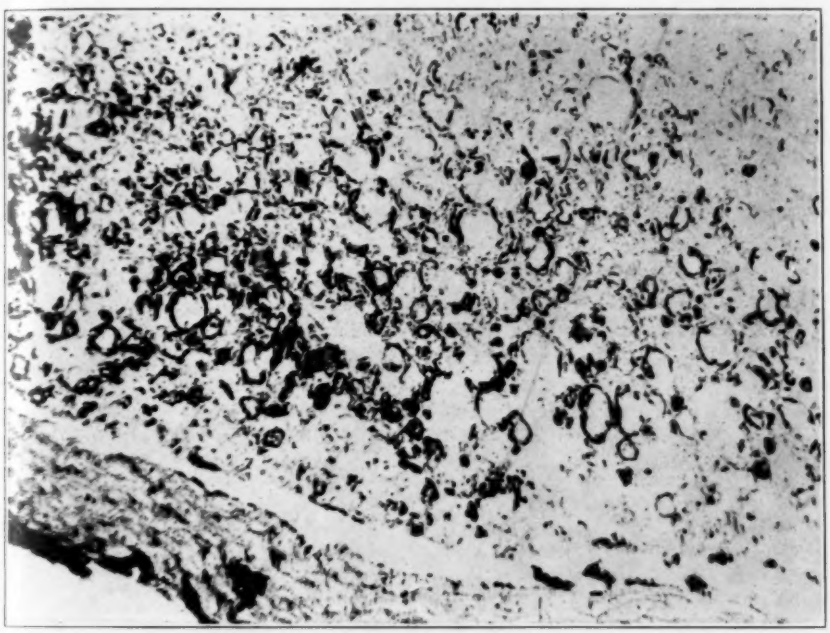

Fig. 5.—Thirty hours after the trauma; degeneration of the axis cylinders and myelin sheaths. Many nerve fibers have disappeared; marked osmic reduction. Fixation in Flemming fluid; Mallory stain.

extremely enlarged protoplasm and nucleus. Some of the neuroglia cells showed osmic inclusions. The meshes of the connective tissue reticulum were distended and in many places broken. The axis cylinders were widely deformed, enlarged and here and there granular (fig. 6), while the osmic acid reduction of the myelin sheaths was diffuse and more pronounced. In fact, the black degenerative spots were scattered throughout the white matter, partly surrounding the axis cylinder, partly occupying the nerve fiber itself and partly free in the section as a result of the breaking down of the myelin sheaths. Figure 7 shows the details of osmic acid reduction which here and there was intense.

The blood vessels showed thickened walls, and their cellular elements showed slight hypertrophy of the cytoplasm with a fairly active nucleus. No

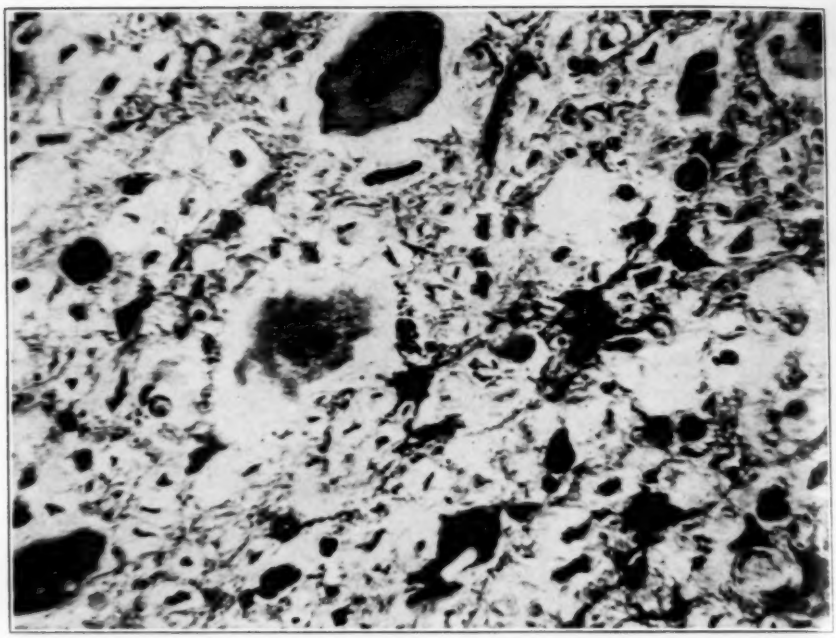

Fig. 6.—Seventy hours after the trauma; extreme enlargement of the axis cylinders which are in an advanced stage of degeneration. Note the granulosity of the axons and the neuroglia reaction. Mallory stain.

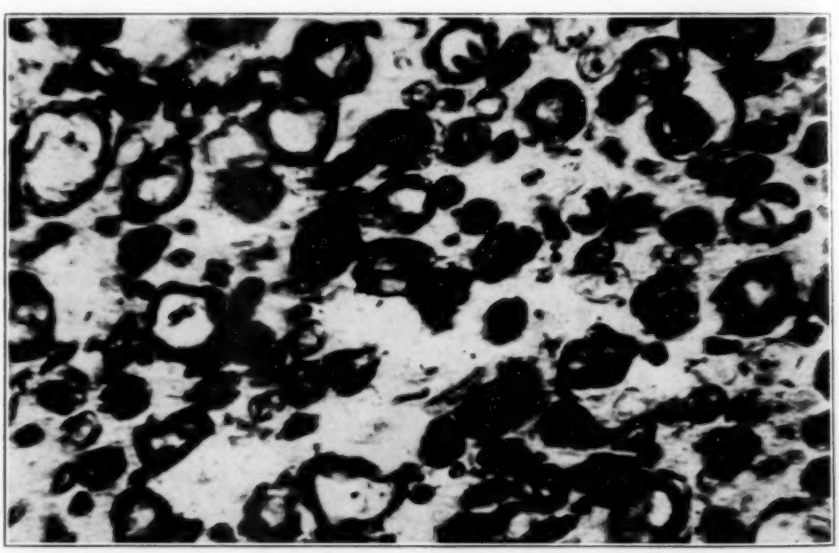

Fig. 7.—Seventy hours after the trauma; intense osmic acid reduction; intense degeneration of myelin sheaths which appear as more or less deformed black rings. Fixation in Flemming fluid; no counterstain.

signs of inflammation were present. The nerve cells as usual showed a certain degree of condensation of the Nissl bodies, but as a rule no signs of acute lesions, swelling or displacement of the nucleus and no chromatolysis. A few prolongations of nerve cells were fragmented and in a stage of more or less advanced degeneration.

The central canal was widely dilated and the lining epithelium was hypertrophic. No cavities were seen, however, in either the gray or the white matter. Small areas of necrosis were scattered throughout the organ. The degenerative process was more pronounced along the periphery of the spinal cord.

RABBIT 8.—The animal was killed ninety-six hours after concussion.

Histologic Examination.—The degenerative process was widely diffuse and markedly intense. Degenerated axis cylinders were scattered throughout the section in both the peripheral and the central areas. The gray matter was the seat of a diffuse disintegrative process showing irregular outlines but no definite cavities.

The detailed examination showed great disturbance of the histologic structure of the framework, the meshes of the reticulum being widely dilated, some of them empty and others containing either enlarged and deformed axis cylinders or residual fragments of reduced osmic acid. The latter was unusually intense, and large, dense black spots were encountered throughout the section, mostly disconnected. The intensity of the degenerative process varied from region to region. In this case the posterior columns were the most severely damaged, the axis cylinders having undergone intense degenerative changes.

The neuroglia reaction was highly pronounced, the cells being diffusely enlarged and the prolongations unusually evident. Numerous cells were free and showed a tendency to become globular, assuming transitory forms leading to the "mobile abraüm-cell." The blood vessels showed thickening and relaxation of their walls. The cellular elements were hypertrophic, and some of them were seen free between the different layers of the walls, contributing to the formation of mesodermic "abraüm-cells."

RABBIT 9.—The animal was killed six days after concussion.

Histologic Examination.—Briefly summarized, the changes noticed at this period were represented by pronounced neuroglia reaction and by more diffuse reaction of the mesodermal cells. The neuroglia cells in a few places were of the monster type with large cytoplasm and occasionally two nuclei. The blood vessels showed loose walls and hyperplasia of the cellular elements. These cells, in the proximity of the necrotic areas, were markedly hypertrophic, and some of them appeared free in the surrounding of the blood vessels.

The nerve fibers showed the same type of degenerative lesions, although the process was much more advanced. The axis cylinders appeared swollen, extremely deformed and contained one or more vacuoles. The vacuolization seemed to be connected with the more advanced period of degeneration; some of the nerve fibers appeared highly vacuolated, while others were poorly stained and granular. This granular aspect is distinctly seen in one of the axis cylinder in figure 6. Occasionally the axis cylinder was replaced by a neuroglia cell which belongs to the category of the cells described by Jakob as present along the nerve fibers and as being in charge of directly removing the waste products of the degenerated fibers. The osmic acid reduction was pronounced here, although it must be recalled that, as a rule, the two types of osmic and albuminous degeneration of the axis cylinders are independent of each other. Many axis cylinders had already undergone the maximum of the degenerative process and no trace of them was detected.

Compared with the axis cylinders, the nerve cells showed less degenerative changes, although some of them, especially in the anterior horn, showed reaction of the acute type following lesions of the axis cylinder. A few of the cells showed an extremely displaced nucleolus, occasionally even in the cytoplasm. The degenerative changes of the spinal roots and their zones of entrance were still noticeable.

COMMENTS

Lesions following concussion of the spinal cord are noticeable as early as one hour after the trauma.

The lesions of the axis cylinder appear to be primary as they are present at such an early stage, independently of lesions of the myelin sheath. They are especially represented by swelling and deformity. The lesion of the myelin sheaths is revealed by the osmic acid reduction twelve hours after the concussion.

The intensity of the lesions is related partly to the intensity of the trauma and partly to the duration of the lesions. In fact, in my cases I have never found the typical cavities of necrosis that other authors have been able to find. The lack of such severe lesions might presumably be connected with the lesser intensity of the traumatic action. Comparing these lesions with those due to the action of a bullet on the vertebrae, one finds in the latter that cavities are frequent and sometimes of great extent. The vibratory and traumatic action of a bullet is incontestably much more violent and localized than the action of the percussive agent used in my experiments.

It is reasonable, then, to establish a correlation between the intensity of the trauma and the severity of the lesions from a general as well as from a detailed point of view. Indeed, the primary enlargement of the axis cylinder as well as its deformity must be connected with the intensity of the traumatic action independently of the secondary changes following the eventual interruption of the nerve fiber. I am inclined to believe that although most of the nerve fibers are enlarged and deformed as a result of the traumatic action, some of them are injured as a result of the interruption of the axis cylinder. Cajal has already described in secondary degeneration of nerve fibers such characteristic bolas or swelling of the terminal portion. But the difference might consist in the fact that while in the secondary reaction the enlargement is terminal, usually localized at the end of the central extremity, in the traumatic lesion the enlargement is seen all along the nerve fiber in the traumatic area and not localized to some of the nerve fibers. I am then inclined to correlate most of the diffuse enlargement of the nerve fibers with a primary lesion of the axis cylinder, independent interruption.

The osmic acid reduction of the myelin sheaths might be of a primary origin as well as the result of the interruption of the nerve fiber. Presumably the osmic degeneration encountered at the earlier period of

twelve hours after the trauma is the result of primary chemical changes provoked by the traumatic vibration, while the diffuse osmic degeneration of the later stages is a combination of primary and secondary changes. Presumably the dissociation between the albuminous type (swelling, granulosity and deformity of the axis cylinder) and the osmic type of degeneration of nerve fibers is the result of the prevailing of primary or secondary lesion, the albuminous type corresponding much more to the primary lesions.

The evaluation of the osmic type of degeneration is still more difficult, as it is well known that even in the primary degeneration, as for instance in pernicious anemia, osmic reduction is also encountered although not extensively. However, this study of the earliest stage establishes the primary nature of the lesions of the nerve fibers, although the fact should not be neglected that the secondary lesions following eventual interruption of the nerve fibers makes difficult sharp distinction between the lesions belonging to the primary and secondary types of degeneration.

The reaction of the neuroglia cells appears in the very early stage, and after the first hour enlargement of the cell bodies is evident. The neuroglia reaction increases in intensity with the duration of the lesions.

The removal of the waste products does not seem to take place before a certain time has elapsed. It is after from eighteen to thirty hours that the first small inclusions are seen in the neuroglia cells. After this preliminary period the activity of the neuroglia cells increases, and the removal of the disintegration products becomes more and more pronounced. However, the presence of "Gitterzellen" of both ectodermal and mesodermal origin is limited. The participation of the mesodermal cells in the process of removal of waste products is important, but in many of the cases described their participation is sluggish; only in the later periods of four and five days, beginning hypertrophy and hyperplasia of the mesodermal cells are encountered. This slight mesodermal participation is proportionate to the moderate intensity of the degenerative process of the nervous parenchyma. No areas of hemorrhage or large areas of severe necrosis were encountered which would necessitate the intervention of an active removing process. Removal of the waste products is then primarily reserved for the ectodermal cells, both fixed and mobile elements, which slowly elaborate the material before releasing it to the mesodermal cells called into action later. In cases of more severe lesions, the mesodermal participation would certainly have been much more active, and free reticulogranular cells would have been seen in earlier stages. The participation of the mesodermal cells must, then, be related to both the duration and the intensity of the pathologic process.

The lesions of nerve cells are of moderate degree when compared with the lesions of nerve fibers. As with the axis cylinders, the nerve

cells also present lesions that I am inclined to consider as primary and independent of the secondary axonal reaction. These lesions are as follows: broken outlines of the cells, fragmentation of the prolongations, conglutination of the neurofibrillar reticulum and displacement of the nucleolus. The presence of these lesions in the very early stages (one to four hours after the concussion) is in favor of their primary nature, and, on the other hand, the histologic picture is different from the reaction following lesion of the axon. Occasionally, here and

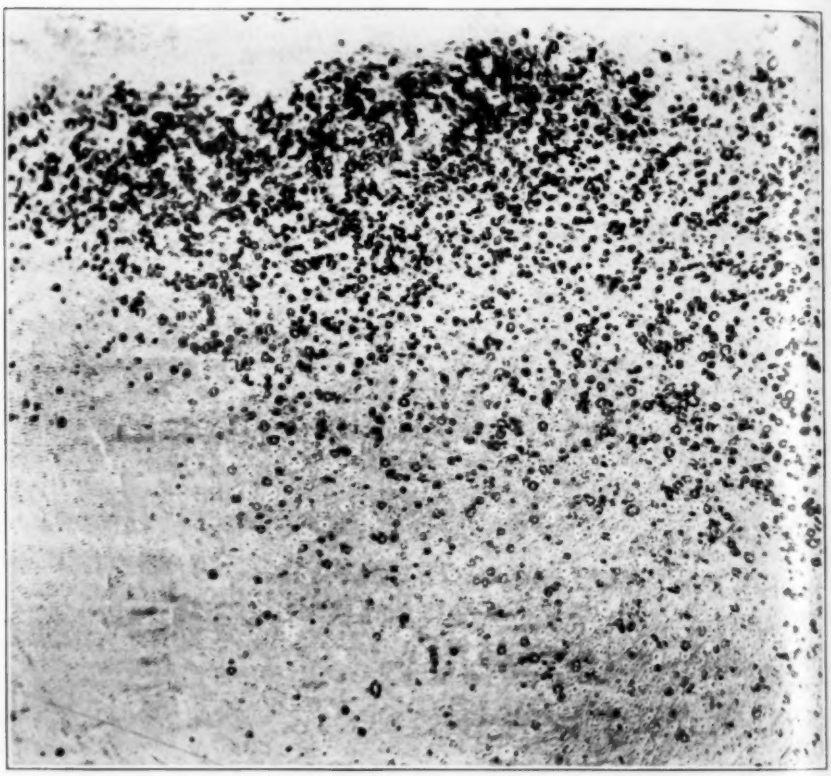

Fig. 8.—Ninety-six hours after the trauma; peripheral degeneration—"Randdegeneration"—which can be found also in earlier stages. The degeneration process decreases in intensity toward the central portion of the cord. Fixation in Flemming fluid; no counterstain.

there, presumably following lesions of the anterior roots, a few cells are seen showing the typical characteristics of the reactive phase.

I must recall that the displacement of the nucleolus within the nucleus and even into the cytoplasm has already been described in my previous work on traumatic necrosis of the spinal cord, and that Ingvar has found in his experimental work a frequent displacement of the nucleolus along the periphery of the nucleus, especially in the spinal

ganglion cells. On the other hand, it must not be forgotten that occasionally in other pathologic processes the same behavior of the nucleolus can be found. The fact that this is so common in concussion, however, indicates that displacement of the nucleolus is correlated to traumatic reaction.

The formation of cavities in the white matter must be directly related to the intensity of the trauma. Cavities have been found almost constantly in the severe lesions following concussion caused by a bullet as well as in experimental lesions following prolonged centrifugalization. Undoubtedly the vibratory and concussive results of these agents are, especially the first, far more severe than those of simple concussion. Although cavities have been found by others using the same type of percussion, the absence of typical cavities in my experiments presumably may be related to the moderate intensity of the trauma.

The pathogenesis of the lesions following concussion of the spinal cord might be interpreted on the basis of two factors: the first represented by the shock of the cerebrospinal fluid, transmitted all around the spinal cord, and the second represented by the vibratory action of the tissues. At the seat of the concussion a liquid wave originates which acts locally against the spinal cord, as a foreign body causing a rim degeneration (as seen in figure 8), and is then transmitted along the spinal cord above and below the area of percussion. The liquid wave propagates itself along the different septums, where it develops a concussive action of the same type as the local one. The result which follows is a dilatation of the sulci, especially of the sulcus medianus anterior, which sometimes is accompanied by laceration of the central gray matter. The second factor, represented by the vibration which takes place in the bony tissue, is then transmitted to the cerebrospinal fluid and to the medullary parenchyma; this varies in intensity according to the strength of the percussion. Every component of the organic tissues possesses a vibratory index which gives it a certain resistance to vibratory action, but as soon as this limit is overstepped, the tissue undergoes disintegration of variable intensity. Because of their length and slenderness, it is probable that the nerve fibers are subject to the pernicious effects of intense vibration more than are the nerve cells. The blood vessels, and this explains the rarity of hemorrhage, appear to possess the highest resistance. The vibration of the fluid can be transmitted also to the central ependymal canal (through the foramina of Luschka and Magendie). This possibility is indicated by the frequent lesions of the central canal and by the cases in which the lesions were more pronounced in the inner layers of the white matter close to the gray matter.

The lesions of the nerve roots are presumably the combined result of the action of the cerebrospinal fluid and the displacement of the spinal cord, producing traction on the spinal roots.

OBSTRUCTION OF THE LONGITUDINAL SINUS*

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Within a comparatively short time at the Mayo Clinic, necropsy has revealed four cases of thrombosis of the superior longitudinal sinus. In only one case was involvement of the sinus definitely considered; in no case was such a diagnosis made.

REPORT OF CASES

CASE 1.—*Thrombosis of the superior longitudinal sinus secondary to osteomyelitis of the skull, with death and necropsy.*

History.—A woman, aged 30, came to the Mayo Clinic, Dec. 21, 1923, complaining of pain and swelling of the left side of the cheek and of swelling of both eyelids. Four months previously she had suffered from pain in the left side of the cheek, which an operation on the left maxillary sinus, November 5, relieved for two weeks. The left eye, left side of the cheek and right eye then swelled, and a fortnight later the left side of the cheek and the left lacrimal sac were incised. Four days before admission, slight pain in the left ear was followed by purulent aural discharge.

Condition and Course.—The patient was acutely ill, with edema of the left side of the cheek and of both eyelids. Besides the discharging sinuses of the left cheek and lacrimal sac, there was a perforation of the left membrana tympani, through which pus was draining. A roentgenogram revealed destruction of the left malar and nasal bones. The daily temperature varied between 97.6 and 101 F. and the pulse between 85 and 125. On Jan. 10, 1924, a radical operation on the frontal sinus revealed infected granulation tissue in the sinus and sequestration of the nasal, ethmoid and maxillary bones. Three days later, the temperature began to show frequent and extensive fluctuations. On January 21, the patient complained of numbness of the entire right side of the body and slight weakness. Within forty-eight hours, she became dull and noncooperative, and manifested right upper monoplegia with weakness in the right lower extremity, right hemianesthesia, cervical rigidity and Kernig's sign bilaterally. The following day a convulsion, involving the left side, was followed by disorientation. At this time engorgement of the left retinal veins, with blurring of the left optic disk, was noted. The patient died, January 30, the temperature being 105 F.

Necropsy.—Purulent thrombophlebitis of the superior longitudinal sinus extending to the right lateral sinus and associated with thrombosis of both jugular veins, purulent exudate over the superior surface of the brain, and necrosis of the left frontal bone were found.

Comment.—The symptoms and signs referable to the initial illness made it difficult, if not impossible, to recognize any congestive phenomena resulting from occlusion of the longitudinal sinus.

The cardinal points in the neurologic history are hemiplegia and hemianesthesia on the right side, beginning on January 21; mental dulness on January 24;

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* From the Section on Neurology of the Mayo Clinic.

* Read before the Chicago Neurological Society, Chicago, Oct. 28, 1926.

a convulsion involving the left side twenty-four hours later, and stupor on the following day. Weakness of the right upper extremity had progressed to complete paralysis before the first left-side convulsive seizure, so that there was doubt as to whether the attack was or was not of jacksonian character. In view of the fact, however, that the paralysis of the right lower limb was not complete (it was graded 3) on the occasion of the left-sided attack, the possibility of bilateral lesions should have been considered.

It was recognized that there was meningeal irritation and increased intracranial pressure. The stormy onset, rapid pulse and general course contraindicated the presence of a localized collection of pus. Examination of the cerebrospinal fluid, Jan. 24, 1924, revealed only one cell, and excluded at that date meningitis of diffuse distribution. It was finally considered that the underlying neuropathologic change was softening of the brain, of infectious character (fig. 1).

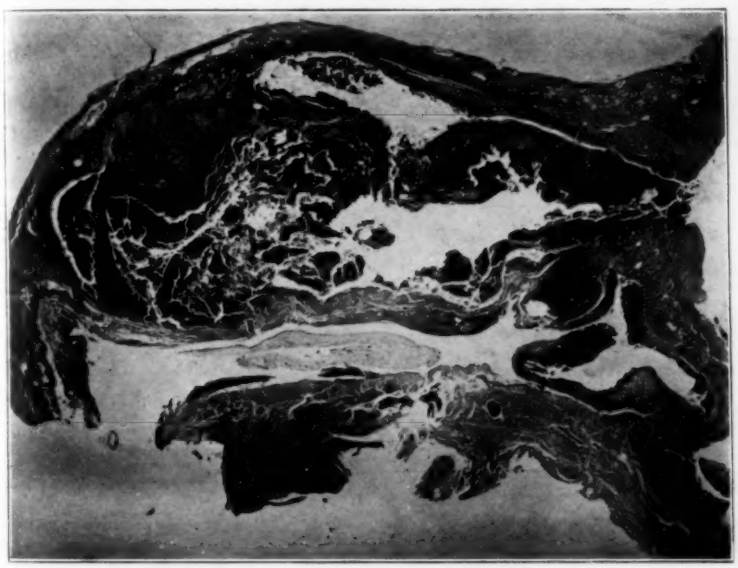

Fig. 1.—Superior longitudinal sinus showing purulent thrombus; × 8.

Case 2.—*Thrombosis of the superior longitudinal sinus secondary to suppurative otitis media, with death and necropsy.*

History.—A woman, aged 33, came to the clinic, Oct. 6, 1926, complaining of pain in the left side of the head. Four months before examination, while seven months pregnant, she suffered from earache on the left side. On the third day myringotomy resulted in a purulent discharge. Three days later, drainage stopped and pain recurred over the entire left side of the head and continued to recur daily. On July 30, one day after the birth of her ninth child, chills and fever set in. Mastoidectomy, performed on August 25, brought relief for several days, when pain recurred over the left side of the head and the left upper jaw, and was associated with emesis.

Condition and Course.—The patient was pale and looked sick. There was a scar from operation behind the left ear, from the bottom of which mucopus exuded. The left membrana tympani was lusterless. Ophthalmoscopic examina-

tion showed choking of both disks with elevation of 1 diopter. On October 10, a convulsion, involving chiefly the right side, was followed by mental confusion and a Babinski sign on the right. On the two succeeding days, there were many similar convulsions with residual hemiparesis of the right side, aphasia and stupor. The patient died, October 14, with a temperature of 107 F.

Necropsy.—Purulent thrombosis of the superior longitudinal sinus with organized thrombosis of the left lateral and sigmoid sinuses, purulent exudate over the superior surface of the left occipital pole, chronic suppurative otitis media, mastoiditis, and necrosis of the adjacent bone were found.

Comment.—The problem in this unusual type of case was to explain the convulsion that involved chiefly the right side and that was followed by mental confusion.

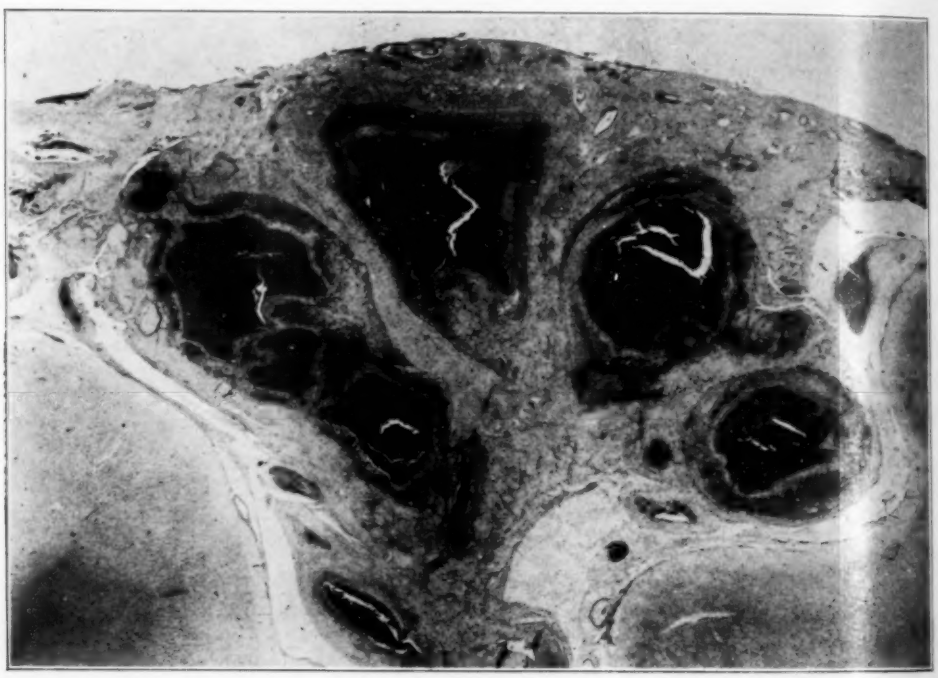

Fig. 2.—Superior longitudinal sinus showing organizing thrombus with multiple abscesses; × 6.

The unsuccessful operations, the continuance of widespread pain and of chills and fever had strongly suggested thrombosis of the sigmoid sinus previously. With the addition of convulsions, during which there was loss of consciousness for a few moments only, and on account of the patient's subsequent confusion, the otologist suggested the possibility of involvement of the superior longitudinal sinus. He was impressed by the clouding of mentality, so unusual with thrombosis of the lateral sinus. The probability of abscess was debated. The majority of cases of abscess secondary to otitis media, however, are of subtle onset and in a large percentage of them bradycardia is found. The pulse rate of from 80 to 160, in association with considerable fever, was more suggestive of widespread inflammatory process (fig. 2).

CASE 3.—*Thrombosis of the superior longitudinal sinus of unknown cause, with death and necropsy.*

History.—A man, aged 28, came to the clinic, April 5, 1926, complaining of convulsions. Ten months previously he had suffered from severe headache for seven days. On the third day he became delirious, vomited several times, and had three convulsions of tonic nature. For the two following months he was weak and unable to read fine print, although his vision for distance was normal. Two months, and again one week, before examination, he had general convulsions.

Condition and Course.—The patient was large and red-faced, with an adenoma of the thyroid gland. The pulse rate was 108. All pulses, including the abdominal aortic, were small. The systolic blood pressure was 140 and the diastolic 90; the basal metabolic rate was + 27. Neurologic examination was objectively negative. Examination of the cerebrospinal fluid, April 12, gave negative results; the pressure was 12 cm. Twenty-four hours later the patient complained of severe headache. On the third day a convulsion involved the left foot, leg and thigh, in that order. The attacks continued to recur and finally involved the left upper extremity. On the fifth day the patient's face was cyanotic; he was stupid, and hemiplegia of the left side and left homonymous hemianopia were present. Lumbar puncture at that time revealed yellow fluid under 10 cm. pressure. Convulsive seizures were repeated at short intervals. On the seventh day the patient became comatose, and he died, April 21, with a temperature of 107.6 F.

Necropsy.—Thrombosis of the longitudinal sinus from the superior frontal gyrus to the torcular herophili was found. There was hemorrhagic softening of the right side of the brain from the superior frontal gyrus to the calcarine fissure, and of the left side of the brain chiefly in the region of the precentral and postcentral gyri.

Comment.—This patient had what appeared to have been an adenoma of the thyroid gland with hyperthyroidism. Kaliebe[1] has reported a somewhat similar case in a woman who had exophthalmic goiter and tabes. So far as I am able to ascertain, this is the second case of this nature to be reported with hyperthyroidism.

The anomalously small pulses throughout the body were striking, the more so when it was learned that two other members of the same family had died from a somewhat similar cerebral condition. The explanation of the severe headache with delirium and convulsive attacks, of two isolated convulsions, and of severe headache followed by jacksonian attacks, hemiplegia and stupor was a difficult diagnostic problem. The spinal fluid was clear on the occasion of the first examination and yellow five days later. Evidence of inflammatory disease was not present, nor was there any increased intracranial pressure. The jacksonian attacks began in the left foot and involved successively the left leg, thigh and trunk. A number of hours after the onset of the first attacks, involvement of the left upper extremity, the neck and the face occurred. Cerebral hemorrhage, presumably of arterial origin, was diagnosed. The arterial distribution, however, is such that multiple and extremely selective lesions would have to be predicated in order to bring about such a syndrome. In the absence of data suggesting inflammatory disease or tumor, and in view of the improbability of arterial cause, a lesion in the venous system would have been the most logical assumption. Had the idea of venous affection come into consideration, thrombosis of the longitudinal sinus might have been seriously considered (fig. 3).

1. Kaliebe, Hans: Autochthone Sinusthrombose bei einem Falle von Morbus Basedow und Tabes, Med. Klin. **2**:1929, 1913.

CASE 4.—*Thrombosis of the superior longitudinal sinus with death and necropsy.*

History.—A woman, aged 21, was brought to the clinic, Jan. 24, 1925. Six months previously she suddenly experienced extremely severe right occipitocervical headache, which was associated shortly with vertigo and vomiting. This syndrome recurred with diminishing frequency during the ensuing five months. Several days after the onset of the headache, she complained of diplopia. Three weeks prior to examination, there was a severe recurrence of the syndrome, with stupor and incontinence.

Condition and Course.—The patient was acutely ill and drowsy, with bloated face, swollen eyelids, and dilated frontal veins. Fundoscopic examination showed choking of the optic disks, with elevation of 2 diopters bilaterally, hemorrhages and exudates. There was paresis of conjugate ocular movements upward and laterally. Cervical rigidity, slight incoordination and diminished speed in the

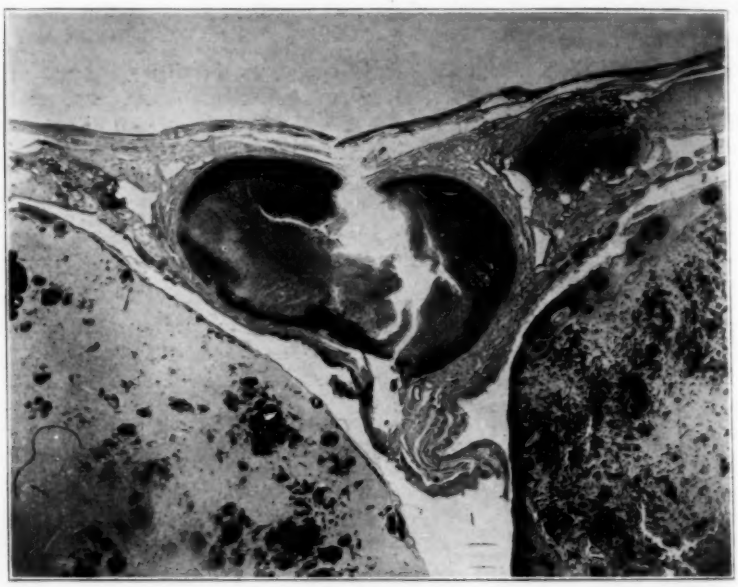

Fig. 3.—Superior longitudinal sinus; × 10.

extremities of the right side were the only other neurologic abnormalities. Movements of the head often induced and always aggravated vertigo. The patient returned home, where she gradually improved and gained 20 pounds (9 Kg.). In May and in July, 1925, the syndrome of headache, vertigo and vomiting recurred and incapacitated her on each occasion for ten days.

On reexamination, July 27, 1925, she looked dejected; the eyelids were puffy and contained dilated veins. The right eye showed proptosis of mild degree. The optic disks were choked and were elevated 2 diopters. The left patellar and achilles reflexes were slightly exaggerated. Lumbar puncture yielded clear fluid under 23 cm. pressure. A ventriculogram was negative. The patient died, Aug. 7, 1925.

Necropsy.—There was thrombosis of the superior longitudinal sinus extending into the medial halves of both lateral sinuses. The thrombus was organized throughout its entire course.

Comment.—The diagnosis in this particular case turned on a rational explanation of episodes of abrupt onset of headache, vertigo and vomiting, associated with edema of the eyelids, dilated frontal veins and choked disks. There was evidence of increased intracranial pressure. The fluctuating course suggested at once the possibility of tumor of the third or fourth ventricle. An attempt was not made to explain the congestive phenomena of the eyelids and forehead. Edematous eyelids should suggest fracture of the skull, infectious processes in and about the orbit, thrombosis of the cavernous sinuses and thrombosis of the longitudinal sinus. There was no history of injury nor of any inflammatory lesion. The absence of infection and the duration and character of the symptoms and signs excluded thrombosis of the cavernous sinuses.

When this patient returned for reexamination, with clinical evidence of regression rather than progression, it seems strange indeed that autochthonous thrombosis of the longitudinal sinus did not suggest itself (fig. 4).

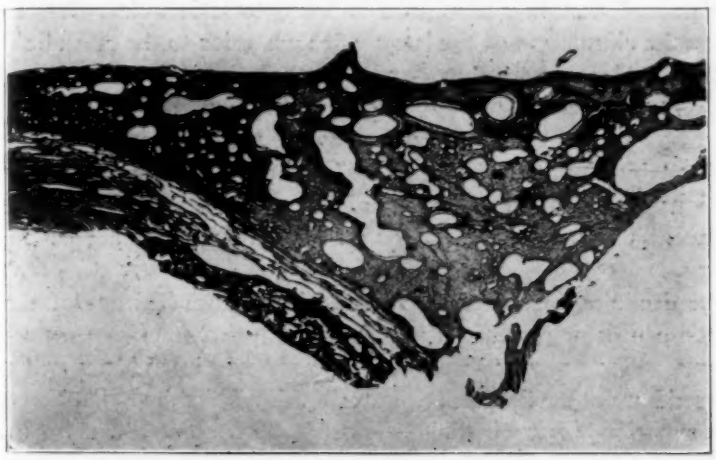

Fig. 4.—Confluens sinum (torcular herophili); × 8.

COMMENT

Direct trauma and neoplasm may also result in occlusion of the sinus. Hershey's case [2] was that of a girl, aged 8, who was struck at the vertex in such a way that a triangular fragment of bone lacerated the superior longitudinal sinus. Digital compression stopped the flow of blood. Several attempts to elevate the fragment were unsuccessful, owing to excessive hemorrhage. Under expectant treatment the wound healed, and the patient survived without further evidence of intracranial disturbance. This phase of the subject has been described in detail by Holmes and Sargent.[3]

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2. Hershey, D. W.: Case of Obstruction of the Superior Longitudinal Sinus, Boston M. and S. J. **61**:336, 1859.

3. Holmes, Gordon, and Sargent, Percy: Injuries of the Superior Longitudinal Sinus, Brit. M. J. **2**:493, 1915.

A review of all supratentorial operations performed at the Mayo Clinic between Jan. 1, 1910, and Oct. 15, 1926, revealed only five cases, all endotheliomas, in which there was occlusion of a sinus. The transverse sinuses were occluded in two cases; the confluens sinum or torcular herophili in one case, and the longitudinal sinus exclusively in two cases. In two of the three cases in which the longitudinal sinus was involved, occlusion was neoplastic, and in the third the tumor had invaded the lumen of the sinus and was associated with a canalized thrombus. In this group of cases there were no symptoms or signs referable to obstruction of the longitudinal sinus. This is probably due to the insidiousness of involvement, to the widespread and free anastomosis, and to the limited extent of this type of obstruction. The situation is somewhat analogous to resection of moderate-sized portions of the sinus. Adson [4] has observed that this procedure is asymptomatic unless the resection impairs the circulation of the large veins posterior to the rolandic fissure.

It is evident, then, that extensive thrombosis is the only mechanism of obstruction of the superior longitudinal sinus commonly producing symptoms. The cases presented illustrate the classification suggested by Tonnelé [5] in 1829. The thrombophlebitic, secondary or infectious group follow infections of bones and soft tissues of the head and face. The primary, bland or autochthonous cases are of doubtful etiology.

The declining incidence of chlorosis has diminished one of the most common causes or conditions associated with thrombosis of autochthonous type. The occurrence of bland thrombosis in children will not be discussed here other than to reiterate Bouchut's dictum [6] that thrombosis of the superior longitudinal sinus is generally present when, for the first time, a child has a convulsion following an acute illness or in the course of chronic debilitating disease.

Case 1 illustrates thrombophlebitis of the superior longitudinal sinus as a complication of an extremely serious infective process. The striking feature in case 2 is the early confusion, stupor and convulsions in the presence of probable thrombosis of the lateral sinus. In case 3, the importance of close analysis of jacksonian seizures is illustrated. In case 4 the diagnosis should have been made if the minds of the examining neurologists had been alert to the probability of autochthonous thrombosis of the longitudinal sinus.

The thrombophlebitic cases were progressive from the first. The autochthonous cases exhibited fluctuating courses. In case 4, evidence

4. Adson, A. W.: Personal communication to the author.

5. Tonnelé: Maladies des sinus veineux de la dure-mère, Arch. gén. de méd. (series 1) **19**:455, 1829.

6. Bouchut, E., quoted by Bertier, J.: La thrombose médicale des sinus de la dure-mère, Arch. gén. de méd. **198**:313, 1907.

of increased intracranial pressure and the fluctuating course led to a diagnosis of ventricular tumor.

It is interesting to speculate as to whether, in this condition, choked disks of moderate or considerable severity indicate integrity of the walls of the venous channels. If this is true, the converse would indicate hemorrhagic softening and alter the prognosis for the worse. These reflections are prompted by case 4, in which definitely choked disks were associated with an intact brain, and in case 3 in which normal optic disks accompanied marked hemorrhagic softening of the brain.

The number, variety and possible combinations of symptoms depend on the type, size and site of the thrombus, the peculiarities of anastomosis of the cerebral veins, and the ability of the cardiovascular apparatus to establish competent collateral circulation.

CONCLUSIONS

1. In the absence of meningitis, the early onset of apathy or stupor in a patient with evidence of thrombosis of the transverse sinus secondary to suppurative otitis media generally indicates infectious thrombosis of the superior longitudinal sinus by retrograde extension, especially if associated with choked disks and convulsions.

2. When the probable presence of tumor or of inflammatory disease can be excluded, jacksonian seizures, showing progression from one foot to the other, as in Shelden's case,[7] or beginning in the foot and gradually involving the homolateral upper extremity, suggest impairment of the circulation of the cerebral veins and probable thrombosis of the superior longitudinal sinus.

3. Abrupt onset of symptoms of increased intracranial pressure, which follow a fluctuating course, should bring to mind the possibility of thrombosis of the superior longitudinal sinus as well as ventricular tumor. The absence of the element of progression after a fair length of time, or actual regression of symptoms, is suggestive of thrombosis of the superior longitudinal sinus. If the syndrome is associated with edema of the eyelids and dilatation of the veins of the eyelids and forehead, and if fracture of the skull, orbital and periorbital infections and thrombosis of the cavernous sinuses can be excluded, the diagnosis is established.

DISCUSSION

DR. LEWIS J. POLLOCK: I would like to ask whether, when the spinal fluid was obtained, a Queckenstedt test was made, and whether that suggested the diagnosis.

DR. ROY GRINKER: At the Michael Reese Hospital, since 1923, there have been some cases of involvement of the longitudinal sinus, all of which have

7. Shelden, W. D.: Personal communication to the author.

been associated with involvement of the other sinuses, especially the lateral. One case followed an abscess of the occipital lobe, one after venipuncture of the superior longitudinal sinus, and the others were secondary to meningo-encephalitis. These cases revealed fairly well organized thrombi. In thinking over the histories, with reference to Dr. Doyle's statement about stupor and convulsions, I recall that the notes on the charts stated that all the patients, toward the last at any rate, were in profound stupor, if not in coma. In none of the patients was there a choked disk, and in none were there localized neurologic signs except in one case in which there was weakness of both upper extremities. The abscess of the occipital lobe involved the longitudinal sinus, apparently by direct extension of the abscess to the superior fissure. None of the cases were diagnosed, and I am sure that the outline that has been presented will make one think more of the possibility of this diagnosis.

Dr. W. A. Jones, Minneapolis: I should like to report the case of a woman, aged 62, who, two and one-half years ago, while visiting friends and sitting at the table, suddenly cried out. She had what she called "mental collapse;" she was unable to comprehend or appreciate what was going on about her, and the attack was accompanied by convulsive movements and pain in the head. After this she developed marked aphasia and weakness of the right side, which varied in its severity from time to time. Gradually the aphasia improved with an occasional return, but for two years the speech was continuously halting and she was unable to deliver herself in comprehensive terms. She still has a little weakness of the right side, particularly when she has a cold or when she is ill from other causes, but it does not last. She uses the right hand and arm without difficulty except that she complains of peculiar sensations, which are common to the hemiplegic person. It seems likely from the symptoms that a diagnosis of thrombosis of the superior longitudinal sinus or of the lateral sinus would explain the condition. She evidently had all of the symptoms described by Dr. Doyle, including involvement of the face and eyelids and the peculiar flat line of the face, but she did not have any convulsive movement or twitching of the arm or leg or suggestive chain of symptoms; even now at times she has a little halting in speech when embarrassed.

Dr. Doyle: A Queckenstedt test is made routinely at the clinic on all patients on whom lumbar puncture is performed. The only case in this group in which examination of the cerebrospinal fluid was not made was case 2. As McEwen pointed out in 1893, autochthonous cases generally involve the azygos sinuses, and thrombophlebitic cases the paired sinuses. He also reported a case of secondary thrombosis, in which recovery occurred following surgical treatment. The case just recorded by Jones was almost certainly one of thrombosis of the superior longitudinal sinus. Buzzard has reported a somewhat similar case in which recovery took place. It has been shown experimentally in animals that occlusion of the larger sinuses frequently is not followed by symptoms and is not incompatible with life.

STUDIES OF METABOLISM IN EPILEPSY

II. THE SUGAR CONTENT OF THE BLOOD *

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Fellow in Medicine of the National Research Council during the greater portion of this research

WITH THE ASSISTANCE OF MARIE O'CONNOR, B.S., AND MARGARET BELLINGER, B.S.

BOSTON

When sufficient insulin is administered to cause the sugar content of the blood to fall sharply to the vicinity of from 45 to 50 mg. per hundred cubic centimeters of blood, a severe reaction usually ensues. In animals, this reaction is accompanied by motor phenomena that are usually described as convulsions. Such convulsions are presumed to be the direct result of the existing hypoglycemia. Furthermore, various authors [1] have found that, under electrical stimulus, irritability of the nerve increases when the blood sugar has been lowered with insulin. These facts raise the question whether persons who are subject to recurring convulsions show abnormal concentration of sugar in the blood.

The observations so far reported are without much value because of the small number of patients examined. Thus, Heidema [2] found hyperglycemia in two of five epileptic patients. Normal values were obtained by Kooy [3] in eight patients and by Weston [4] in ten. Hypoglycemia was found by Burgh, Pryde and Walker [5] (65 mg.) in one of four cases,

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* From the Department of Neuropathology, Harvard Medical School, the Department of Medicine, Massachusetts General Hospital, and the Thorndike Memorial Laboratory, Boston City Hospital. This research was made possible through a grant by the Committee on Epilepsy, New York City. This paper is no. 51 of a series of studies in metabolism from the Harvard Medical School and allied hospitals. The expenses have been defrayed in part by a grant from the Proctor Fund of the Harvard Medical School for the study of chronic diseases.

1. Behrendt H., and Hopmann, R.: Ueber nicht tetanoide Erregbarkeits Veränderungen, Klin. Wchnschr. **3**:2233 (Dec. 2) 1924. Waltner, K.: Insulin und galvanische Erregbarkeit, Klin. Wchnschr. **4**:168 (Jan. 22) 1925. Greisheimer, E. M.: Irritability and Blood Sugar, Am. J. Physiol. **72**:213 (March) 1925.

2. Heidema, S. T.: Blutzuckerbestimmungen bei psychiatrischen und neurologischen Patienten, Ztschr. f. d. ges. Neurol. u. Psychiat. **48**:111, 1919.

3. Kooy, F. H.: Hyperglycemia in Mental Disorders, Brain **42**:214 (Oct.) 1919.

4. Weston, P. G.: Analyses of the Blood of Insane Patients, Arch. Neurol. & Psychiat. **3**:147 (Feb.) 1920.

5. Burgh, D.; Pryde, J., and Walker J.: The Blood Sugar in Cases of Epilepsy, Brit. M. J. **1**:232 (Feb. 9) 1924.

and by Schwab [6] (40 mg.) in one of ten. In a short paper in which he states neither the number of patients examined nor the measurements of blood sugar found, Wladyczko [7] reported that eighteen epileptic patients with hypoglycemia showed improvement during the daily oral administration of sugar. Normal values were found by Shaw and Moriarty [8] in five children and by Holmström [9] in twenty adults. Josephs [10] found hypoglycemia (from 37 to 65 mg.) in four children in whom vomiting and convulsions were associated. He believes that convulsions in these cases were of hypoglycemic origin. However, his patients showed acidosis as well as hypoglycemia, and the evidence presented does not implicate one more than the other. In forty cases of epilepsy, Wuth [11] found blood sugar values between 60 and 118 mg. with an average of 90 mg. per hundred cubic centimeters of blood. In forty-five cases, Weeks, Renner, Allen and Wishart [12] obtained values between 46 and 125 mg. Labbé [13] has reviewed the older literature dealing with diabetes and epilepsy. He concludes that diabetic epilepsy, though rare, exists, but is the result of acidosis rather than of hyperglycemia.

MATERIAL AND METHODS

We have measured the sugar content of the blood of 267 epileptic patients. Half of these were inmates of the Monson State Hospital. Half of the patients were attendants of the nerve clinics of the Massachusetts General and the Boston City hospitals. All of the patients were suffering from recurring seizures of unknown origin. They were about equally divided between the two sexes. Only a few were below 15 or

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6. Schwab, S. I.: Diagnostic Value of Blood Sugar Curves in Neurology, Arch. Neurol. & Psychiat. **8**:401 (Oct.) 1922.

7. Wladyczko, S.: La cure sucrée dans l'épilepsie, Presse méd. **33**:1475 (Nov. 4) 1925.

8. Shaw, E. B., and Moriarty, M.: Hypoglycemia and Acidosis in Fasting Children with Idiopathic Epilepsy, Am. J. Dis. Child. **28**:553 (Nov.) 1924.

9. Holmström, R.: Blutzuckerbestimmungen bei Epileptikern, Upsala Läkaref. Förh. **29**:17 (Jan. 15) 1924.

10. Ross, S. G., and Josephs, H. W.: Observations on the Metabolism of Recurrent Vomiting, Am. J. Dis. Child., **28**:447 (Oct.) 1924. Josephs, H. W.: Fasting as a Cause of Convulsions, ibid. **31**:169 (Feb.) 1926.

11. Wuth, O.: Untersuchungen über die körperlichen Störungen bei Geisteskranken. Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie, Berlin, Julius Springer, 1922.

12. Weeks, D. F.; Renner, D. F.; Allen, F. M., and Wishart, M. B.: Observations on Fasting and Diet in the Treatment of Epilepsy, J. Metabol. Res. **3**:317, 1923.

13. Labbé, M.: Diabetes Mellitus, chapter VIII, New York, William Wood & Company, 1922.

over 50 years of age. About one half of the patients were taking phenobarbital in moderate doses. Working with animals, Ellis and Barlow [14] and Weiss [15] have reported that derivatives of barbituric acid, in doses sufficient to produce anesthesia, cause temporary alteration in the blood sugar level. We have seen no observations concerning the effect of moderate doses of phenobarbital on the level of blood sugar in man. Presumably it has little or no effect, for we obtained practically the same measurements of blood sugar in our patients who were taking phenobarbital as in those who were not taking it. Except in a few instances, as shown on the charts, blood was drawn in the morning before breakfast. Because of the rapid loss of glucose from blood on standing, it was hemolized immediately (within fifteen minutes) after withdrawal. Because the use of excess oxalate causes increased glycolysis in shed blood,[16] only sufficient oxalate to prevent clotting was used. Blood was taken from a vein of the arm with the arm relaxed. The tourniquet was removed before blood was withdrawn. In order to prevent undue pain, with possible consequent increase of blood sugar, sharp, small-caliber needles were used. Blood was drawn from most of these patients on numerous occasions, a circumstance that would minimize any tendency to hyperglycemia from excitement. Glucose was measured by the method of Folin and Wu.[17] The sugar tube, as modified by Rothberg and Evans,[18] was used during the latter part of the research. From one to twelve measurements were made on each patient. Including a series of observations concerning blood sugar curves to be reported elsewhere, we have made approximately 2,000 measurements of blood sugar in epileptic persons.

INDIVIDUAL MEASUREMENTS

Five hundred and nine measurements of blood sugar were made in 267 patients. In order to save the space of tabulation, the results are presented graphically (chart 1). Inspection of the figure shows that, although extreme measurements are 232 and 63 mg. per hundred cubic centimeters of blood, the great majority of the determinations lie within the commonly accepted limits of normal: from 80 to 120 mg. per

14. Ellis, M. M., and Barlow, O. W.: Barbital Narcosis, J. Pharm. & Exper. Therap. **24**:259 (Nov.) 1924.

15. Weiss, S.: Anesthesia Induced by Barbituric Acid Derivatives with Special Reference to Blood Sugar Changes, Proc. Soc. Exper. Biol. & Med. **23**:363 (Feb.) 1926.

16. Birchard, D. E.: Loss of Sugar in Oxalated Blood, J. Lab. & Clin. Med. **8**:346 (Feb.) 1923.

17. Folin, O., and Wu, H.: A System of Blood Analysis, J. Biol. Chem. **41**: 467 (March) 1920.

18. Rothberg, V. E., and Evans, F. A.: A Modified Folin and Wu Blood Sugar Method, J. Biol. Chem. **53**:443 (Dec.) 1923.

hundred cubic centimeters of whole blood. In only one instance did fasting blood sugar exceed 150 mg. This patient was evidently diabetic, as both the blood and the urine contained a large amount of sugar. In no case was the blood sugar as low as it usually is when a severe hypoglycemic reaction occurs.

It is becoming increasingly evident that "epilepsy" is a symptom rather than a disease entity. If this is true, it is possible that the presence of abnormality of metabolism in only a small proportion of epileptic patients would be of etiologic importance in these particular patients. Of the measurements recorded in chart 1, approximately 15 per cent were outside the commonly accepted limits of normal: 4 per cent were above 120 mg., and 11 per cent were below 80 mg. of sugar

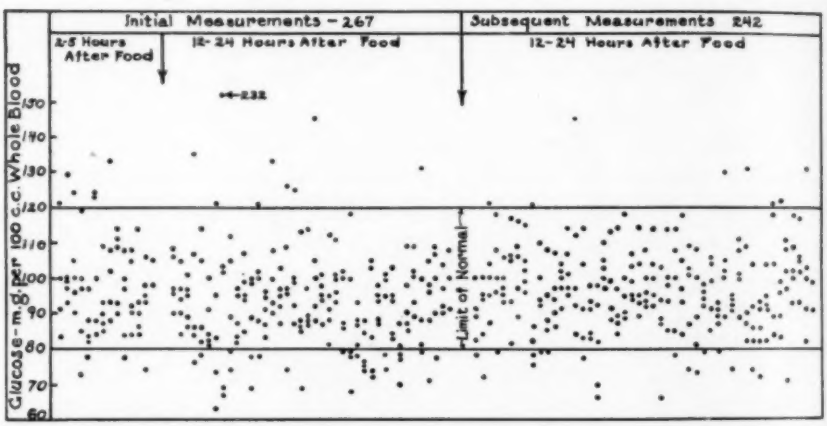

Chart 1.—Five hundred and nine measurements of blood sugar in 267 patients. Each dot represents a single measurement. The ordinate shows concentration of sugar in blood (milligrams per hundred cubic centimeters of whole blood). The abscissa has no significance except that measurements are divided into two groups showing first and repeated determinations. Sixty-six of the initial measurements were made after breakfast. Blood for all others was taken from twelve to twenty-four hours after food was given.

per hundred cubic centimeters of blood. It is important to know if this distribution of measurements differs materially from the distribution in a group of healthy persons. Table 1, illustrated by chart 2, makes such a comparison. The values for epileptic persons comprise 430 measurements made under fasting conditions in 201 of our patients. The group of normal persons consists of 431 single measurements collected from the literature by Gray,[19] with the addition of forty determinations from our own records. Chart 2 shows that the curves representing the distribution of sugar values in the two groups are roughly parallel.

19. Gray, H.: Blood Sugar Standards, Arch. Int. Med. **31**:241 (Feb.) 1923.

The greatest frequency of blood sugar concentration was around 90 mg. for our patients and around 100 mg. for the normal persons, but the difference is too slight to be of significance. Our patients also showed fewer low values than the group of normals. It is possible that with some of the measurements reported in the literature due care was not taken to prevent loss of sugar after withdrawal of blood. Inspection of figures 1 and 2 makes it evident that fasting blood of persons subject to recurring convulsions does not show abnormal concentrations of sugar.

TIME RELATION TO CONVULSIONS

Blood for the measurements recorded was drawn without reference to convulsions. It is possible that blood sugar is normal in the period between seizures but abnormal immediately before or after. Thus, Kersten [20] measured the blood sugar of patients at frequent intervals

TABLE 1.—*Distribution of Measurements of Blood Sugar in Normal and Epileptic Persons*

Blood Sugar, Mg. per 100 Cc.	Normal*		Epileptic†	
	Number	Per Cent	Number	Per Cent
36 - 65	30	6.4	1	0.2
66 - 75	35	7.4	25	5.8
76 - 85	67	14.2	69	16.0
86 - 95	113	24.0	141	32.9
96 - 105	127	27.0	117	27.1
106 - 115	72	15.3	50	11.6
116 - 125	20	4.2	17	4.0
126 and over	7	1.5	10	2.3
Total.....	471	100.0	430	99.9

* Single measurements of 431 persons collected by Gray in the literature with the addition of forty of the authors' measurements.
† Four hundred and thirty measurements made on 201 persons having recurrent convulsions.

during the day. He presents eighteen curves. Four of these in which blood was drawn on the days when seizures did not occur did not show any fluctuations of the blood sugar level. In contrast with these, fourteen curves plotted for days when seizures occurred presented marked variations. The lowest measurement recorded was 40 mg. and the highest 220 mg. Although, in the main, low blood sugar values were found in the half hour or hour preceding seizures and higher values during the several hours following the seizures, this relationship was not constant. For example, the blood sugar fell in one case after an attack of petit mal to 40 mg., and in another after a slight seizure to 42 mg. In other curves, marked fluctuations in level occurred without immediate relationship to seizures. Kersten attributes the fluctuations observed to increased secretion of epinephrine. Curiously enough, one finds no statement as to whether food was withheld from patients during the days

20. Kersten, H.: Ergebnisse zur Frage des elementaren Krampfes, Ztschr. f. d. ges. Neurol. u. Psychiat. **63**:48, 1921.

of observation. Another possible criticism is the use of Bang's micromethod of analysis. In this method capillary blood is taken from the lobe of the ear on blotting paper. The use of such a small amount of blood increases the error of measurement. Holmström [9] took blood at intervals during the day from three patients who were given food every hour. The time relations of food and blood taking are not stated. He also used Bang's micromethod. He states that seizures come at the low point on these curves. In contrast to the observations of Kersten, the recorded fluctuations are slight. Not more than 24 mg. (i. e., from 80 to 104 mg.) separate lowest from highest values. Holmström considers that these variations are secondary to perturbations of the sympathetic system. In one instance, blood was taken every half minute. Successive

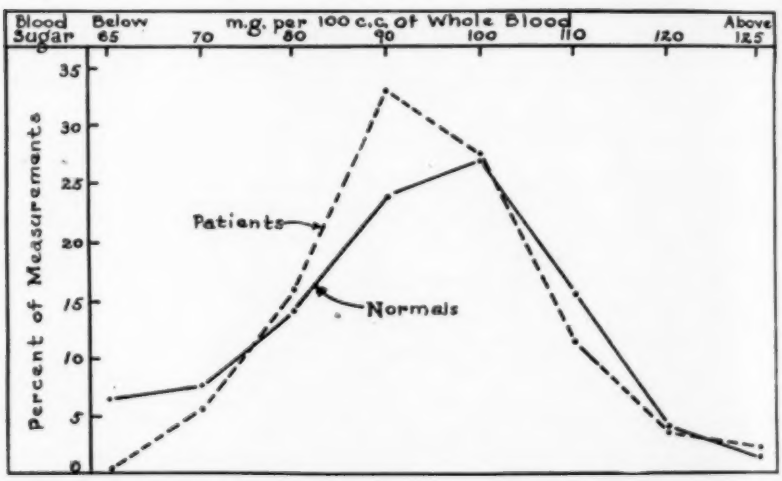

Chart 2 (illustrating table 1).—Distribution of blood sugar measurements in 471 normal persons (solid line) compared with distribution of 430 measurements of 201 epileptic persons (broken line). The ordinate represents the percentage of the total group. The abscissa represents the concentration of sugar in the blood grouped by decades. The lowest values are at the left; the highest at the right. It will be seen that measurements from patients are more nearly within the commonly accepted limits of normal than measurements from the normal persons.

measurements varied as much as 21 per cent during seizures, against 5 per cent variation in an interparoxysmal period. Frisch and Walter [21] reported daily measurements of the blood sugar of three patients during eight periods of from four to eight days' duration. The authors stress the occurrence of high sugar values from one to three days before a seizure. However, on only two occasions was hyperglycemia present (137 and 139 mg.). The thirty-nine measurements made were too few

21. Frisch, F., and Walter, K.: Untersuchungen bei periodischer Epilepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **79**:367, 1922.

to permit conclusions. The same may be said of the fifteen measurements made by Wuth [11] on four patients.

Seizure is preceded by hyperglycemia, according to Barlocco,[22] who does not present supporting data. Vollmer [23] made hourly measurements of blood sugar in two cases. In one of these, concentration of sugar fell from 92 to 72 mg. preceding a seizure. Pezzali [24] did not find any significant variation in blood sugar before, during and after seizure in four cases. Metcalf and Moriarty [25] reported a case of convulsions occurring in nephritis in which blood sugar was greatly elevated (up to 312 mg.) during the seizures. They also have data concerning blood sugar and seizures during ketosis in children with epilepsy.[26] These pieces of evidence are too fragmentary and contradictory to permit the drawing of conclusions.

We have had unusual opportunity to observe the relationship between the blood sugar level and the frequency of seizures through studies of patients during fasting treatment. In these cases the troublesome factor of food intake did not enter. On theoretical grounds—because of the previously mentioned relationship of hypoglycemia to convulsions and increased irritability of the nerves, and because of the infrequency of epilepsy and diabetes in the same person—one would expect low sugar levels in the blood to be accompanied by increased frequency of seizures. On the contrary, during fasting, when blood sugar is maintained at a low, constant level, we find that seizures are less frequent. Detailed data concerning blood sugar during six fasting periods have been presented elsewhere.[27] We failed to find parallelism between the daily incidence of seizures and the level of circulating glucose. Chart 3 shows such a lack of parallelism in one of our cases. During the nineteen day period in which no seizure occurred, blood sugar was increased on one occasion to 126 mg. by the injection of epinephrine and on another occasion to 203 mg. by the ingestion of glucose, without a return of the spells. It is true that the number of seizures and the level of blood sugar both fell

22. Barlocco, A.: Ricerche sul ricambio intermedio dell'n, indicano, NaCl., glucosio, calcio, colesterina, e grassi nell'epilessia, Riforma med. **38**:580, 1922.

23. Vollmer, H.: Zur Pathogenese der genuinen Epilepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **84**:546 (July) 1923.

24. Pezzali, G.: Ricerche sul contenuto del sangre in azoto (residuo) closuri, colesterina, grassi, glucosi, indicano, e calcio nell'epilessia, Riforma med. **39**:433 (May 7) 1923.

25. Metcalf, K. M., and Moriarty, M.: Blood Chemical Findings During Convulsions, Am. J. Dis. Child. **31**:65 (Jan.) 1926.

26. Talbot, F. B.; Metcalf, K. M., and Moriarty, M. E.: A Clinical Study of Epileptic Children Treated by Ketogenic Diet, Boston M. & S. J. **196**:89 (Jan. 20) 1927; Epilepsy; Chemical Investigations of Rational Treatment by Production of Ketosis., Am. J. Dis. Child. **33**:218 (Feb.) 1927.

27. Lennox, W. G.: Chemical Changes in the Blood During Fasting, Arch. Int. Med. **38**:553 (Nov.) 1926.

at the beginning of the fast. We believe, however, that changes in the level of blood sugar were merely secondary to changes in alkalinity of blood, and that the latter is the factor of importance. The evidence for this will be presented in a separate publication.

In addition to the foregoing, we have evidence gained by artificial alteration of the blood sugar level of epileptic patients. In about 450 instances, we have caused a sharp increase of blood sugar by means of ingestion or intravenous injection of glucose. Contrary to the reports of Wladyczko [7] and Cuneo,[28] who thought that their patients were benefited by the feeding of glucose, seizures in our patients seemed to be neither more nor less frequent because of such temporary alteration in the sugar level of the blood. One of our patients, for example, was having frequent seizures of a myoclonic nature. On successive days, we gave her glucose by mouth and 10 units of insulin subcutaneously. For a two hour period on these successive days, the number of seizures was as follows: two control days, twenty-two seizures each; following the ingestion of glucose (with blood sugar up to 160 mg.), twenty-three seizures; following the giving of insulin (with blood sugar depressed to 72 mg.), thirteen seizures.

The preceding data, as well as most of that referred to in the literature, deal with the question of the blood sugar level several days or hours before or after a seizure. The question next arises whether there are changes in concentration of blood sugar during the seizure itself. The evidence in the literature, as we have seen, is fragmentary and conflicting. On several occasions, we have not found any change in the level of sugar in blood drawn during attacks of petit mal. One would, however, expect changes to attend the muscular exertion, the asphyxia and the increased intracranial pressure which accompany a convulsion. Rakestraw [29] found an increase in the blood sugar after from ten to fifteen minutes of exercise. He, as well as Levine, Gordon and Derick [30] and Burger and Martens,[31] found that hypoglycemia may follow prolonged exertion. Various authors have shown that asphyxia causes marked increase in the blood sugar, though the rôle played by the factors of anoxemia,

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28. Cuneo, G.: Studi sulla pathogenesi dell'epilessia: IV. Della prota albumose e delle sue relazioni con le crisi epileptiedre et e con ce crisi insuliniche, Arch. di Path. e Clin. Med. **22**:72, 1926; V. L'azione convulsivante ed: suoi fatori patogenetici, Riv. sper. di freniat. arch. ital. per le malatt. nerv. e ment. **49**:65, 1925.

29. Rakestraw, N. W.: The Effect of Muscular Exercise upon Certain Common Blood Constituents, J. Biol. Chem. **47**:565, 1921.

30. Levine, S. A.; Gordon, B., and Derick, C. L.: Some Changes in the Chemical Constituents of Blood Following a Marathon Race, J. A. M. A. **82**:1776 (May 31) 1924.

31. Burger, G. C. E., and Martens, J. C.: Der Blutzuckergehalt bei Muskelarbeit, Klin. Wchnschr. **3**:1860 (Oct.) 1924.

increased carbon dioxide content of the blood and increased secretion of epinephrine is not yet clear. Tychowski and Crowell [32] have recently demonstrated that hyperglycemia accompanies increase of intracranial pressure.

In table 2, illustrated by chart 4, we present comparative measurements of blood sugar during a series of convulsions in an epileptic patient, and during convulsions simulated by a healthy person. The patient was a young man who stated that he had eaten little if any food for several days. In the six hours preceding the period of observation, detailed in table 3, he had had five convulsions. His convulsions were severe, lasted two or three minutes, and were marked by a prolonged tonic phase with intense cyanosis. On three occasions blood was drawn during a convulsion, near the end of the clonic phase.

TABLE 2.—*Measurements of Blood Sugar in Epileptic and in Simulated Convulsions*

Epileptic Patient J. R.			* Healthy Subject W. L.		
Time	Relation to Convulsion	Blood Sugar, Mg. per 100 Cc.	Time	Relation to Convulsion	Blood Sugar, Mg. per 100 Cc.
2:52 p. m.	During convulsion.....	81	12:40 p. m.	Before.....	94
2:58 p. m.	8 minutes after.....	79	1:05 p. m.	Before.....	95
3:08 p. m.	18 minutes after.....	80	1:30 p. m.	Before.....	93
3:25 p. m.	During convulsion.....	80	2:05 p. m.	Before.....	93
3:30 p. m.	5 minutes after.....	78	2:07 p. m.	During tonic phase....	94
3:42 p. m.	17 minutes after.....	80	2:11 p. m.	During clonic phase....	107
3:57 p. m.	32 minutes after.....	78	2:16 p. m.	5 minutes after.....	105
4:10 p. m.	During convulsion.....	73	2:35 p. m.	24 minutes after.....	105
4:29 p. m.	19 minutes after.....	78	3:03 p. m.	52 minutes after.....	99
4:47 p. m.	37 minutes after.....	68	3:06 p. m.	During tonic phase....	96
5:20 p. m.	70 minutes after.....	77	3:09 p. m.	During clonic phase....	99
8:30 a. m.*	90 minutes after.....	78	3:15 p. m.	6 minutes after.....	94
			3:45 p. m.	36 minutes after.....	95

* Blood taken the following morning before food was given. There had been seven convulsions during the night.

With the healthy subject, the experimental period was begun five hours after a light breakfast. The subject simulated the tonic phase of a convulsion for a period of approximately forty-five seconds. During this time pressure was maintained on the jugular veins; the subject did not breathe, and held his arms and legs rigid. He became cyanotic and experienced paresthesia of the hands. Blood was withdrawn at the end of this period, after which the patient resumed breathing and jerked his arms and legs vigorously at a rate of approximately 150 times a minute, for three minutes, when another sample of blood was withdrawn. The simulated convulsions were continued longer than the epileptic convulsions in order to compensate for their comparative lack of intensity.

Chart 4 shows that the concentration of sugar in the blood increased after the first simulated convulsion, but not after the second. In contrast,

32. Tychowski, W. Z., and Crowell, C.: Pressure on the Central Nervous System in Its Relation to Hyperglycemia, Arch. Int. Med. **37**:567 (April) 1926.

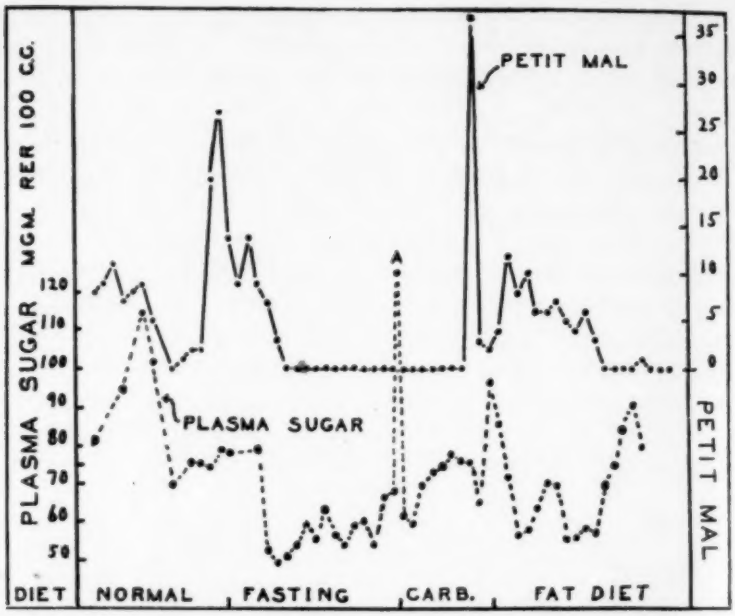

Chart 3.—Comparison of frequency of seizures (solid line) and blood sugar level (dotted line) in epileptic patient H. G. The ordinate represents the daily number of attacks of petit mal and concentration or sugar in the blood. The abscissa represents days of observation. Each dot stands for a day. The measurement *A* followed subcutaneous injection of epinephrine. Invariably, blood was drawn at least twelve hours after food was given. Various experimental procedures that influence frequency of seizures are not represented on the chart.

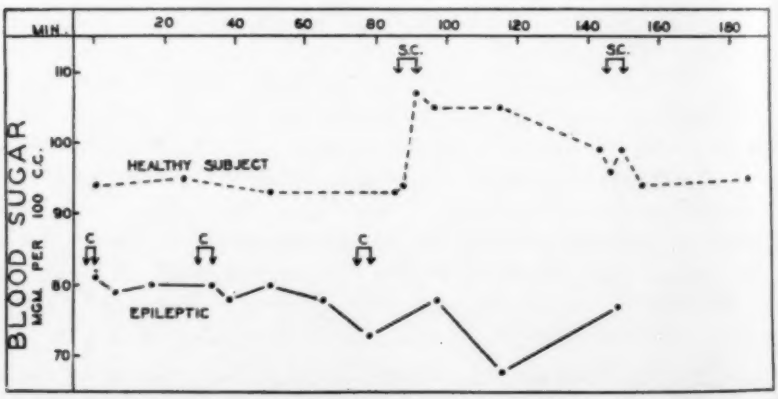

Chart 4.—Concentration of blood sugar with relation to convulsions. The abscissa represents minutes, the ordinate, milligrams of sugar per hundred cubic centimeters of whole blood. Dotted line, healthy person; solid line, epileptic person. The arrows, together with *S.C.*, mark the periods of simulated convulsions, and arrows with *C*, the periods of real convulsions.

the real convulsions of the epileptic person were either not attended by change or were attended by a decrease of blood sugar. It will be noted, also, that the general level of the blood sugar was lower in the patient than in the normal person. These observations suggest that whether or not blood sugar increases with convulsions depends on the amount of available glucose in the body. An isolated convulsion in a well fed person will be attended by a rise in blood sugar, whereas a series of convulsions in a person not recently fed quickly exhausts the available glycogen reserves, and the blood sugar becomes lower and lower with each successive seizure. The hypoglycemia of this patient is of the same order as the hypoglycemia of the exhausted Marathon runners examined by Levine.[30] The clinical application of this observation is apparent. Patients having serial seizures or in status should be given fruit juice or glucose at frequent intervals in order to combat the exhaustion that accompanies hypoglycemia.

COMMENT

Though the foregoing evidence denies any more than a purely passive rôle to circulating sugar in the events attending convulsions, it is evident that a knowledge of the mechanism of the hypoglycemic reaction might lead to a better understanding of other convulsive phenomena. Yet in the case of reaction from insulin, the exact relationship of sugar level to the reaction is not clear. Various authors have shown that hypoglycemia induced by agents other than insulin may not be accompanied by a reaction, or that the occurrence or severity of a reaction following the injection of insulin may not bear any relation to the blood sugar level. In man, as in the case reported by Smith,[33] sugar may be absent from the blood without the occurrence of marked motor phenomena. Brain [34] believes that the reaction from insulin in rabbits is not a convulsion, but rather a disturbance in equilibrium due to reduction of afferent impulses from the labyrinth, an explanation to which MacLeod [35] offers certain objections. In a recent monograph, MacLeod has summed up the evidence concerning the action of insulin. He ascribes convulsions to rapid changes in the tension of glucose within the nerve cell. This view receives support from the observations of Forshay [36] that the general

33. Smith, M.: An Unusual Blood Sugar Finding During an Insulin Reaction, Boston M. & S. J. **195**:663 (Sept. 30) 1926.

34. Brain, W. R.: The Nervous Symptoms of Insulin Hypoglycemia in Rabbits Contrasted with the Convulsions Induced by Cocaine, Quart. J. Exper. Physiol. **16**:43 (March) 1926.

35. MacLeod, J. J. R.: Carbohydrate Metabolism and Insulin, London, Longmans Green & Co., 1926.

36. Forshay, L.: Observations upon the Action of Insulin with Special Reference to the Cause of the Condition Known as Hypoglycemia, Am. J. Physiol. **73**: 470 (July) 1925.

symptoms of the reaction from insulin accompany the fall in the sugar content of the red cell rather than of the plasma. On the other hand, MacLeod points out that the symptoms of hypoglycemia are much like those of anoxemia and that convulsions may be caused by a locking of oxygen within the tissues with consequent deficient oxygen content of the blood entering the brain.

Our observations have been concerned solely with the concentration of glucose in the circulating blood of epileptic persons. It is well known that glucose passes quickly between the blood and the tissues and that there is equilibrium (according to Donnan's law) between the sugar of the blood and of other fluids of the body. One might assume, therefore, that measurements of blood sugar give fairly accurate knowledge of concentration of sugar throughout the body. Observations by Asher and Takahashi,[37] however, open new possibilities with regard to carbohydrate metabolism in the brain. They found that methods which reduce the glycogen of liver and muscle by 90 per cent reduce the glycogen of the brain by only 20 per cent. If the injection of insulin in rabbits was not followed by convulsions, there was a slight increase of carbohydrates in the brain, whereas if convulsions resulted, glycogen was reduced by 80 per cent. A somewhat similar reduction of glycogen of the brain followed convulsions induced by picrotoxin. The brain of a patient dying in tetanic convulsions did not show glycogen. From these observations, Asher and Takahashi conclude that the storage of carbohydrate in the brain is peculiarly stable and that it is drawn on only by conditions that favor a state of exaggerated excitability of the central nervous system. Whether such a loss of glycogen is the cause or the effect of the convulsions they do not say. Obviously this and other phases of carbohydrate metabolism and their relation to the convulsive phenomena require further investigation. In a subsequent paper, we shall present evidence concerning the effect of the ingestion of glucose on the concentration of the sugar of the blood of epileptic persons.

CONCLUSIONS

Study of 267 epileptic patients fails to show abnormality in the concentration of sugar in the blood or any direct relation between the blood sugar level and seizures. Increase of blood sugar during convulsions would seem to depend on the presence of available glucose in the body.

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37. Takahashi, K.: Hypoglykämie und Kohlenhydratstoffwechsel des Zentralnervensystems, Klin. Wchnschr. **3**:1914 (Oct. 14) 1924; Ueber experimentelle Kohlenhydratverarmung und den Kohlehydratstoffwechsel des Gehirns, Biochem. Ztschr. **154**:444, 1924. Asher, L., and Takahashi, K.: On the Experimental Production of Lack of Carbohydrates and on the Carbohydrate Metabolism of the Central Nervous System, Proc. Soc. Exper. Biol. & Med. **22**:238, 1925.

STUDIES OF METABOLISM IN EPILEPSY

III. THE BLOOD SUGAR CURVE *

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The possibility that there may be abnormality in carbohydrate metabolism in persons subject to convulsive disorders is suggested by the fact that convulsions and increased irritability of nerves accompany hypoglycemia produced by insulin in animals, by the reported marked diminution in glycogen content of the brain accompanying convulsions, and by the occasional clinical reports of patients who seemed to be better or worse following variation in the carbohydrate content of the diet. In a previous paper [1] we have discussed these considerations, and from a study of 267 patients have concluded that persons suffering from so-called epilepsy present no abnormality in the concentration of glucose in the circulating venous blood and that, in the events which accompany convulsions, blood sugar plays only a passive rôle.

It is possible, however, that blood drawn from a fasting person may show normal concentration of sugar, and yet that there may be distinct abnormality in the carbohydrate metabolism, as revealed by the height to which blood sugar rises following the ingestion of a certain amount of glucose. For example, in diabetes mellitus following ingestion of glucose, concentration of sugar in the blood is abnormally high and prolonged. Such a patient is said to present a high blood sugar curve—or, less exactly, a low sugar tolerance. This so-called blood sugar test has been used extensively in many clinical conditions. Few observations, however, have been made with respect to epilepsy.

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* From the laboratory of the Department of Neuropathology, Medical School of Harvard University, the Medical Service of the Massachusetts General Hospital and the Thorndike Memorial Laboratory of the Boston City Hospital. This research was made possible through a grant by the Committee on Epilepsy, New York City. This paper is no. 53 of a series of Studies in Metabolism from the Harvard Medical School and allied hospitals. The expenses have been defrayed in part by a grant from the Proctor Fund of the Harvard Medical School for the study of chronic diseases.

1. Lennox, W. G.; O'Connor, Marie, and Bellinger, Margaret: Studies of the Metabolism in Epilepsy. II. The Sugar Content of the Blood, Arch. Neurol. & Psychiat. p. 383 this issue.

A review of the literature concerning postprandial glycosuria in epileptic patients is given by Holmström.[2] Such observations are of little value in judging of the degree of hyperglycemia because of the variation in different patients in the renal threshold for sugar. Kooy[3] found normal sugar curves in eight patients with epilepsy, following the ingestion of a breakfast consisting of bread, butter and milk. Of twelve patients examined, Olmstead and Gay[4] found curves normal in three, high in six, and low in three. Schwab[5] found normal curves in ten patients. Holmström[2] performed sugar curve tests in twenty cases of epilepsy. The majority of these, however, were made following the subcutaneous injection of epinephrine. In seven instances he measured the sugar curve following ingestion of 100 Gm. of glucose. These curves, he said, were all normal. However, the published charts show that in four of the curves the peak was reached at one and one-half hours, instead of at the half hour or the hour, as is usual. Drury and Farran-Ridge[6] found normal sugar curves in all but one of fifteen epileptic persons. This patient, who presented a steeple shaped curve, had a seizure at the beginning of the test. Wladyczko[7] published charts showing two curves, neither of which was distinctly abnormal.

MATERIAL AND METHODS

In order to have patients who should show as wide a distribution of type as possible, we chose subjects both from the clinics of a general hospital and from an institution giving custodial care. Distribution among institutions of the patients examined was as follows: Attendants of the Nerve Department of the Massachusetts General Hospital, sixty-seven; of the Boston City Hospital, sixteen; private patients, twelve; inmates of the Monson State Hospital for Epileptics, forty-five. We made no effort to segregate a special group of these patients who might be labeled "essential epilepsy." In most of the patients, seizures were of unknown etiology. Detailed study of some of the

2. Holmström, R.: Blutzuckerbestimmungen bei Epileptikern, Upsala Läkaref. Förh. **29**:17, 1924.

3. Kooy, F. H.: Hyperglycemia in Mental Diseases, Brain **42**:214 (Oct.) 1919.

4. Olmstead, W. H., and Gay, L. P.: Study of Blood Sugar Curves Following a Standardized Glucose Meal, Arch. Int. Med. **29**:384 (March) 1922.

5. Schwab, S. I.: Diagnostic Value of Blood Sugar Curves in Neurology, Arch. Neurol. & Psychiat. **8**:401 (Oct.) 1922.

6. Drury, K. K., and Farran-Ridge, C.: Some Observations on the Types of Blood Sugar Curve Found in Different Forms of Insanity, J. Ment. Sc. **71**:8 (Jan.) 1925.

7. Wladyczko, S.: La cure sucrée dans l'epilepsie, Presse méd. **33**:1472 (Nov. 4) 1925.

patients revealed conditions that might account for the convulsions. The influence of such conditions, together with the question of age and mental condition, will be discussed later.

Our method of performing the test was as follows: Venous blood was taken from the patients in the morning before breakfast. Pure dextrose in 33 per cent solution was given in an amount equivalent to 1.5 Gm. per kilogram of the patient's body weight, except that 100 Gm. was ordinarily the largest amount given. When glucose was injected, 0.3 Gm. per kilogram of anhydrous, chemically pure dextrose in 20 per cent solution was given. Blood was withdrawn at intervals of one-half, one and two hours after the glucose was administered. Urine was secured at the end of the two hour period. Patients were all on a mixed diet. Because a ketogenic diet results in an abnormally high blood sugar curve, we have discarded curves obtained from patients who were on a fat diet.

The method of Folin-Wu [8] was used for measuring sugar. Though Folin [9] now states that this method measures a certain amount of sugar other than glucose, he has shown that following the ingestion of glucose, such nonglucose material does not vary. Therefore, although the accompanying figures of blood sugar, as measured by the Folin-Wu method, may not give absolute values for glucose in blood, the curves are of the same form as though only glucose was being measured. We took care to use only sufficient oxalate to prevent coagulation, and to hemolize the blood with water immediately after withdrawal. Urine sugar was measured by the method of Benedict, making use of the pipet devised by Millard Smith.[10]

RESULTS

We have performed tests of the blood sugar curve on 140 epileptic patients. Repeated tests were done on many of these, following both ingestion and intravenous injection of glucose, so that in all we have constructed approximately 400 curves. For the sake of brevity, we shall present in tabular form only the data concerning the curve of each patient which followed the initial ingestion of glucose. Of these 140 curves, a few had been preceded by a previous test in which glucose had been injected intravenously.

In deciding as to the abnormality of the curves obtained, we are under difficulty because of the difference of opinion as to what constitutes a normal curve. If, with Mosenthal,[11] we consider curves the peaks of which are above 160 mg. or below 120 mg. as abnormal, we find that of our 140 initial curves from patients with epilepsy, 37 per

8. Folin, O., and Wu, H.: A System of Blood Analysis. A Simplified and Improved Method for Determination of Sugar, J. Biol. Chem. **41**:367, 1920.

9. Folin, O., and Svedburg, A.: The Sugar in Urine and Blood, J. Biol. Chem. **70**:405 (Oct.) 1926.

10. Smith, Millard: A Micro-Modification of the Method of Benedict for the Quantitative Determination of Reducing Sugar in Urine, J. Lab. & Clin. Med. **7**:3 (March) 1922.

11. Mosenthal, H. O.: The Interpretation of Sugar Tolerance Tests, M. Clin. N. Amer. **9**:549 (Nov.) 1925.

cent are high, 15 per cent are low, and only 48 per cent are normal. Rabinovitch,[12] and Petty and Stoner [13] consider a curve that reaches a peak of 180 mg. or more as abnormal. Thirty-one, or 22 per cent, of our patients have a high curve by this standard. John [14] believes that the criterion of abnormality is not the height to which the curve rises. If at the end of three hours the concentration of sugar has not returned to a normal level, he considers the patient diabetic or prediabetic. Several of our patients belonged in this group—but we did not continue our curve to the three hour point in a sufficient number of cases to permit grouping on this basis.

In classifying our curves, we have used the results tabulated by Gray [15] in his report of observations found in the literature. We define a high curve as one which rises to a peak value of 165 mg. or more, and is above 120 mg. at the end of two hours. A flat curve is one in which the concentration at thirty minutes is not more than 10 mg. above the fasting level. The normal curve is one that does not fall in either of these groups. Judged by this standard, 24 per cent of the initial curves of our patients are high, 6 per cent are flat, and 70 per cent are normal.

HIGH SUGAR CURVES

Before considering the significance of these curves, it is necessary to review the conditions in which abnormally high curves occur. McCrudden,[16] in a recent monograph, has given references to articles in which patients with the following diseases have been reported as exhibiting the diabetic type of blood sugar curve: hyperthyroidism, hypertension, nephritis, gastro-intestinal cancer, cirrhosis of the liver, obstructive jaundice, thrombo-angiitis obliterans, chronic alcoholism, encephalitis, furunculosis, arthritis, myxedema and dyspituitarism, as well as the physiologic conditions of fatigue, obesity, old age and menstruation. With regard to the last condition, however, Okey and Robb [17] have recently reported flatter curves during menstruation than

12. Rabinovitch, I. M.: Blood Sugar Time Curves, J. Clin. Investigation **2**:579 (Aug.) 1926.

13. Petty, O. H., and Stoner, W. H.: Respiratory Quotient Curves in Diagnosis of Diabetes, Am. J. M. Sc. **171**:842, 1926.

14. John, H. J.: Glucose Tolerance—Value in Diagnosis, J. Metab. Research **4**:255, 1923.

15. Gray, H.: Blood Sugar Standards. I. Normal and Diabetic Persons, Arch. Int. Med. **31**:241 (Feb.) 1923.

16. McCrudden, F. H.: A Proposed Method of Selecting Risks Among Individuals with Occasional Slight Glycosuria, Association of Life Insurance Medical Directors of America, 1925.

17. Okey, R., and Robb, E. I.: Studies of the Metabolism of Women. Variations in the Fasting Blood Sugar Level and in Sugar Tolerance in Relation to the Menstrual Cycle. J. Biol. Chem. **65**:165 (Aug.) 1925.

in the intermenstrual period. Since McCrudden's publication, the following conditions have been named as associated with high sugar curves: various infectious diseases (Labbé and Boulin [18]), eczema (Ayres [19]), intestinal intoxication in children (Tisdall, Drake and Brown [20]), early stages of pregnancy (Host [21]), injuries of the head (Davidson and Allen [22]) and acromegaly (Cushing [23]). The following authors have found abnormally high blood sugar curves in certain mental conditions: Kooy,[3] Olmstead and Gay,[4] Drury and Farran-Ridge,[6] Lorenz,[24] Schwab,[5] Schrijver,[25] Barrett and Serre,[26] Cowie, Parsons and Raphael,[27] Henry and Mangam,[28] and Kazanin.[29]

Table 1 and figures 1 and 2 present data concerning the high curves obtained in our patients. With the previously mentioned observations in mind, inspection of table 1 shows that age as a possible factor in our high curves may be eliminated, because the oldest patient was 55 years old. Obesity also is not important, as only one patient, case 33, weighed more than 80 Kg. Nineteen of the patients were women. No record was kept of the presence of menstruation. However, the variable curves with respect to the menstrual period found by Okey and Robb [17] were not outside the range of normal. A more important consideration is that of the mental condition of the patients. The authors already quoted found high curves in various types of mental disease, but not

18. Labbé, M., and Boulin, R.: Troubles de la glyco-regulation au cours des infections, Bull. et mém. Soc. méd. d. hôp. de Paris **49**:1358 (Oct. 30) 1925.

19. Ayres, S.: Glucose Tolerance Reactions in Eczema, Arch. Dermat. & Syph. **11**:623 (May) 1925; Glucose Intolerance Associated with Eczema, California & West. Med. **23**:1560 (Dec.) 1925.

20. Tisdall, F. F.,; Drake, T. G. H., and Brown, A.: Studies on the Carbohydrate Metabolism of Infants, J. Lab. & Clin. Med. **10**:2004 (June) 1925.

21. Host, H. F.: Carbohydrate Tolerance in Pregnancy, Lancet **1**:1022 (May 16) 1925.

22. Davidson, E. C., and Allen, C. I.: Blood Glucose Curve in Head Injuries, Bull. Johns Hopkins Hosp. **37**:217 (Oct.) 1925.

23. Davidoff, L. M., and Cushing, H.: Studies in Acromegaly: VI. Disturbances of Carbohydrate Metabolism, Arch. Int. Med. **39**:751 (June 15) 1927.

24. Lorenz, W. F.: Sugar Tolerance in Dementia Praecox and other Mental Diseases, Arch. Neurol. & Psychiat. **8**:184 (Aug.) 1922.

25. Schrijver, D.: Onderzoekingen over de alimentaire glykaemie bij psychosen in het bijzonder bij dementia praecox, Nederl. Tijdschr. v. Geneesk. **67**: 2656 (June 16) 1923.

26. Barrett, T. M., and Serre, P.: Blood Analysis and Sugar Tolerance in Mental Disease, J. Nerv. & Ment. Dis. **59**:561, 1924.

27. Cowie, Parsons, and Raphael: Insulin and Mental Depression, Arch. Neurol. & Psychiat. **12**:522 (Nov.) 1924.

28. Henry, G. W., and Mangam, E.: Blood in Personality Disorders, Arch. Neurol. & Psychiat. **13**:743 (June) 1925.

29. Kazanin, J.: The Blood Sugar Curve in Mental Disease. II. The Schizophrenic (dementia praecox) Group, Arch. Neurol. & Psychiat. **16**:414 (Oct.) 1926.

apparently in simple deterioration, the condition that some of our patients presented. Mental condition did not seem to influence our curves. Almost all the patients from Monson State Hospital and almost none of the patients of the Massachusetts General and Boston City Hospitals showed marked mental deterioration; yet the proportion of the two groups showing high sugar curves was the same.

In addition to these general considerations, a few of the patients listed in table 1 showed evidence of disease conditions previously mentioned. Subject 6 gave roentgen-ray and spinal fluid evidence of

TABLE 1.—*High Blood Sugar Curves in Thirty-Four Epileptic Patients* *

Number	Sex†	Age	Weight, Kg.	Glucose Given, Gm.	Blood Sugar				Glucose in Urine, Gm.
					Fast	½ Hour	1 Hour	2 Hours	
1	♂	19	53.2	80	95	178	124	124	0
2	♂	37	63.2	95	118	167	167	157	0
3	♂	18	50.4	75	114	174	170	121	0
4	♀	41	44.0	67	94	168	148	143	0.26
5	♂	20	59.5	90	76	172	145	138	0
6	♀	45	56.8	86	74	216	213	125	0.5
7	♀	30	47.5	72	105	133	184	178	1.0
8	♀	21	46.2	70	100	190	182	170	0
9	♀	20	59.4	86	107	176	140	124	0
10	♀	55	74.4	100	108	178	200	148	0.13
11	♂	22	57.4	82	100	146	196	149	1%
12	♀	19	56.2	81	101	112	181	142	1.64
13	♀	49	70.3	103	95	148	188	200	0.5
14	♂	22	69.4	100	98	155	181	138	0
15	♂	26	56.2	82	90	165	176	147	0.9
16	♂	41	77.3	110	91	210	183	124	0
17	♀	34	74.6	112	92	241	241	172	+
18	♂	15	62.8	91	92	144	154	171	0
19	♀	25	50.7	76	133	182	—	211	0
20	♂	28	54.0	81	89	156	—	222	+
21	♀	29	50.0	75	97	210	194	164	—
22	♀	17	46.7	70	100	200	129	123	—
23	♂	16	50.0	75	94	179	143	133	—
24	♀	20	60.8	90	145	147	176	127	0.51
25	♀	47	65.3	95	101	190	200	130	0
26	♂	37	79.1	100	100	165	185	176	2.7
27	♀	18	60.3	43	102	126	185	185	0
28	♂	40	70.0	105	100	202	203	161	+
29	♀	22	42.0	63	121	192	270	164	—
30	♀	14	41.7	66	111	400	200	129	0
31	♀	21	45.4	60	115	164	205	148	0
32	♂	35	65.3	95	100	174	198	186	0.9
33	♀	20	81.3	100	82	147	208	148	0
34	♂	25	60.0	30	229	316	318	295	9

* The peak of the curve was 165 mg. or more, and the two hour value was above 120 mg.
† In this and in the other tables, ♂ indicates male; ♀, female.

tumor of the pituitary gland; subject 10 had exophthalmic goiter; subject 21 gave a family history of endocrine disturbance. The mother had exophthalmic goiter, a brother, myxedema, and a sister died of acute diabetes. Patient 29 had essential hypertension, and patient 34, diabetes. In the remaining twenty-eight patients, the cause of the high sugar curve was not evident.

High sugar curves mean that the rate of absorption of glucose from the intestinal canal is more than equal to the combined rates of oxidation and of storage of glucose in the body. Determination of which of these three factors, or which combination of factors, is responsible in

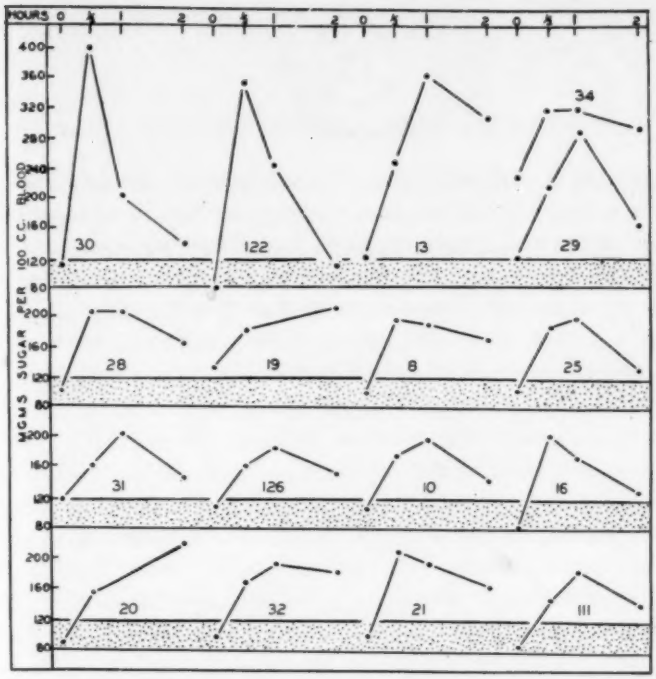

Fig. 1.—Abnormally high blood sugar curves in patients with epilepsy. In this and the subsequent figures, the ordinate represents milligrams of glucose per hundred cubic centimeters of whole blood. The stippled area indicates the commonly accepted normal zone for fasting blood sugar. The abscissa represents hours. The numerals with each curve refer to the number of the patient as listed in tables 1 to 3. Three of the curves are not initial curves. Number 122, though not classified as a high curve because the two-hour blood sugar is below 120 mg., is charted because of its unusual height, 352 mg. Curves of patients 20 and 30 were made several days after resumption of food following a fast.

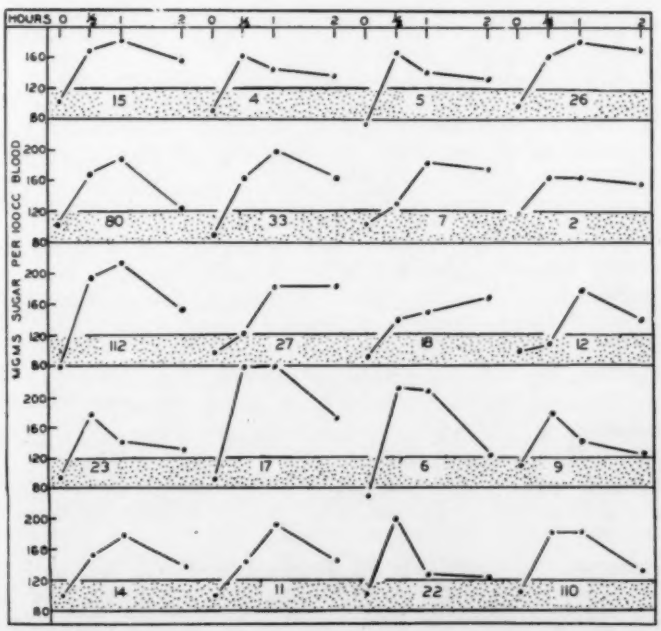

Fig. 2.—Abnormally high blood sugar curves in patients with epilepsy. Three of the curves are not initial curves.

these cases is a difficult matter. Simultaneous study of respiratory quotients, oxygen consumption and blood sugar curves by Linder, Hiller and Van Slyke [30] showed that high curves in nephritis were not due to failure to burn sugar, but to some factor such as retarded glycogen formation. Rabinovitch [31] found that deficient oxidation may be at fault in one diabetic person and deficient storage at fault in another. In our epileptic patients, the possibility of deficient storage might attend abnormalities of the liver. Thom [32] has pointed out the disproportionately small weight of the liver in epileptic persons. Langfeldt [33] has shown that increased acidity of liver cells results in increased glycogenolysis. In epilepsy, however, whatever evidence exists of abnormal acid-base relationship is in the direction of increased alkalinity of the blood. Deficient utilization of glucose might attend disturbance in the function of the endocrine glands, especially the two which have most often been accused of playing a part in epilepsy: the suprarenals and the pituitary. With regard to the latter, Sachs and Macdonald [34] have found that after extirpation of the pituitary gland in dogs, the sugar curve is peculiar in that the peak occurs at the hour, rather than at the half-hour. Twenty-seven of the thirty-four high curves in table 1 exhibit this characteristic. For the whole 140 curves, however, the proportion with the peak at the hour is about the same—32 per cent—as John [14] found in nondiabetic persons. We made a number of sugar curves following injection of epinephrine and of solution of pituitary. Patients with high sugar curves following ingestion of glucose usually had high curves following injection of epinephrine. Evidently these patients had difficulty in disposing of glucose whether it was derived from liver glycogen or was ingested.

Another possible cause for deficient oxidation of the glucose is an acceleration of the rate of blood flow through the muscles, with consequent decrease in the amount of glucose abstracted from the blood. Pemberton [35] has emphasized this possible explanation of the high sugar

30. Linder, G. C.; Hiller, A., and Van Slyke, D. D.: Carbohydrate Metabolism in Nephritis, J. Clin. Investigation **1**:247 (Feb.) 1925.

31. Rabinovitch, I. M.: Simultaneous Respiratory Exchange and Blood Sugar Time Curves Obtained in Diabetic and Non-Diabetic Individuals Following Ingestion of Glucose, J. Clin. Investigation **2**:143 (Dec.) 1925.

32. Thom, D. A.: Abnormal Relation Between Liver and Brain Weights in Forty-Two Cases of Epilepsy, J. Nerv. & Ment. Dis. **43**:442, 1916.

33. Langfeldt, E.: Blood Sugar Regulation and Origin of Hyperglycemias, J. Biol. Chem. **46**:433 (April) 1921.

34. Sachs, E., and Macdonald, M. E.: Blood Sugar Studies in Experimental Pituitary and Hypothalmic Lesions, Arch. Neurol & Psychiat. **13**:335 (May) 1925.

35. Pemberton, R.; Hendrix, B. M., and Crouter, C. Y.: Studies in Arthritis. The Blood Gases and Blood Flow, J. Metab. Research **2**:301, 1922; Arthritis, J. A. M. A. **87**:1253 (Oct. 16) 1926.

curves found by him in patients with arthritis. While making glucose sugar curves, we have often observed venous blood that resembled arterial blood, but we have not found such blood especially associated with high concentrations of blood sugar. Another possible explanation of prolonged hyperglycemia following ingestion of glucose, emphasized by Beeler et al.,[36] is an unduly prolonged absorption of the glucose from the intestinal tract. In many of our cases, however, high curves followed intravenous injection as well as ingestion of the glucose.

In order to check our results, we measured blood sugar curves of twenty-three students who, on physical examination, showed no evidence of organic disease. The results are given in table 4. Five of the twenty-three curves were high. We repeated the test in three of these subjects, and in each the second curve was normal. These students showed evidence of vasomotor instability; e. g., faintness, excessive perspiration and low blood pressure. It is possible that disturbance of

TABLE 2.—*Flat Blood Sugar Curves in Eight Epileptic Patients* *

Number	Sex	Age	Weight, Kg.	Glucose Given, Gm.	Blood Sugar				Glucose in Urine, Gm.
					Fast	½ Hour	1 Hour	2 Hours	
35	♂	25	52.9	76.9	90	96	87	82	0
36	♀	24	58.7	88.5	83	83	69	—	0
37	♀	19	46.7	68.0	91	101	90	83	—
38	♀	21	52.6	79.9	97	98	97	102	—
39	♀	13	58.7	85.5	82	91	81	107	0.48
40	♂	41	84.8	100.0	109	105	101	90	0
41	♂	12	51.8	81.0	100	85	74	105	0
42	♂	21	68.0	99.0	87	92	100	105	0

* The value one half hour after administration of glucose was not more than 10 mg. above the fasting value.

the sympathetic system may be a factor in the initial high curves obtained in some of our patients. This possibility will be discussed more fully presently.

In order to determine the constancy of abnormal conditions, we reexamined many of our patients. Of the thirty-four patients listed in table 1, the test was repeated one or more times in nineteen. On repeated trial, six of these curves remained high, and thirteen, on at least one occasion, became normal. Because we obtained lowering of the sugar curve on repeated trial with nonepileptic subjects, we believe that this interesting observation is not necessarily concerned with epilepsy. Of twenty initially normal curves which were repeated, three became high (table 5).

This variability of curves on repeated trial makes the concise statement of results difficult. If, however, we consider only the patients who presented no evidence of conditions that might account for the

36. Beeler, C.; Bryan, A. W.; Cathcart, E. P., and Fitz, R.: An Improved Alimentary Glucose Tolerance Test, J. Metab. Research **1**:549, 1922.

TABLE 3.—*Normal Blood Sugar Curves in Ninety-Nine Epileptic Patients*

Number	Sex	Age	Weight, Kg.	Glucose Given, Gm.	Blood Sugar				Glucose in Urine, Gm.
					Fast	½ Hour	1 Hour	2 Hours	
43	♀	34	57.8	87	73	142	102	90	0
44	♂	25	54.3	82	74	103	82	69	0
45	♂	32	55.7	82	87	154	133	89	0
46	♂	34	53.3	81	103	136	142	102	0
47	♂	48	62.7	94	93	125	125	112	0
48	♂	39	64.7	97	118	151	124	121	0
49	♀	31	43.2	66	78	147	125	69	Trace
50	♂	10	45.2	70	114	125	114	109	0
51	♂	40	56.8	84	95	133	100	102	0
52	♀	36	47.7	73	78	118	116	108	0
53	♀	19	84.3	126	100	118	99	78	0.22
54	♀	22	66.8	101	85	108	88	95	0
55	♂	24	77.7	116	98	150	163	91	0.42
56	♀	18	46.3	79	93	121	110	89	0
57	♂	49	55.2	83	95	133	114	77	0
58	♂	22	69.2	103	103	140	125	121	0
59	♂	15	58.2	88	83	111	112	87	0
60	♀	19	56.8	88	72	114	93	83	0
61	♀	24	56.8	88	84	124	98	86	0
62	♀	42	50.8	79	88	147	107	90	0
63	♀	21	47.7	72	74	145	144	145	0
64	♀	28	46.8	71	87	125	114	118	0
65	♀	41	50.5	76	104	190	195	97	0.75
66	♀	13	58.6	88	80	158	100	85	0
67	♀	30	52.2	79	100	132	136	108	0
68	♂	31	64.5	96	78	102	73	73	0
69	♀	14	39.8	73	68	159	84	67	0
70	♀	33	69.1	106	79	116	98	100	0
71	♀	23	50.5	76	89	135	91	91	0
72	♀	29	47.3	72	95	120	125	111	0.27
73	♀	34	38.4	59	92	136	88	80	0
74	♂	16	45.4	58	81	141	130	96	0
75	♂	42	71.0	103	89	151	147	108	0.13
76	♂	15	51.3	75	109	140	103	95	—
77	♂	45	112.3	100	94	158	162	114	1.5
78	♂	17	56.7	85	131	152	165	108	—
79	♂	17	79.9	117	82	121	83	80	—
80	♂	16	76.2	111	102	161	135	154	0
81	♀	32	66.0	99	97	129	129	118	0
82	♀	38	66.7	100	100	144	160	137	—
83	♂	17	66.0	96	91	129	132	111	0.86
84	♂	29	67.3	98	77	95	116	76	0
85	♂	15	52.2	79	90	144	85	87	0
86	♂	22	63.5	96	71	100	88	88	0
87	♀	23	49.9	73	92	165	135	118	0
88	♀	15	68.5	100	97	128	93	101	0
89	♀	16	80.7	100	104	132	100	142	0
90	♂	21	71.2	100	109	183	135	108	0
91	♂	46	60.8	89	108	156	168	110	Trace
92	♂	51	72.7	100	118	154	121	95	0
93	♂	23	83.9	100	96	139	117	106	0.6
94	♂	17	72.6	106	95	145	146	133	0
95	♂	41	70.3	100	85	111	133	101	0
96	♂	21	55.6	81	90	120	117	86	—
97	♂	45	61.7	93	97	152	118	99	0
98	♂	25	60.3	91	95	139	130	...	—
99	♂	29	60.0	90	92	137	118	100	0
100	♂	17	64.9	94	105	136	137	108	0
101	♂	30	48.9	76	87	500	114	114	0
102	♀	25	63.2	96	91	154	119	112	0
103	♂	16	59.0	43	98	124	116	86	0
104	♀	24	58.1	84	96	131	122	104	0.18
105	♂	23	64.5	100	69	105	69	69	0
106	♀	29	70.8	100	89	174	118	85	0.42
107	♂	14	55.3	78	113	166	111	116	0
108	♂	15	57.2	86	104	175	100	107	0.6
109	♂	15	54.0	78	88	107	143	133	0
110	♂	30	64.9	94	88	152	144	132	0
111	♀	15	64.0	93	93	156	164	128	0
112	♀	24	59.9	87	87	192	171	102	Trace
113	♀	20	68.9	100	97	126	133	123	—
114	♂	15	49.4	72	97	154	129	111	0
115	♂	15	63.3	95	81	118	108	87	—
116	♂	28	56.0	84	114	152	99	118	0
117	♂	21	60.7	91	95	154	129	98	—
118	♂	17	74.4	109	96	140	130	113	0.12
119	♂	45	69.7	104	86	134	112	87	0

TABLE 3.—*Normal Blood Sugar Curves in Ninety-Nine Epileptic Patients—Continued*

Number	Sex	Age	Weight, Kg.	Glucose Given, Gm.	Blood Sugar				Glucose in Urine, Gm.
					Fast	½ Hour	1 Hour	2 Hours	
120	♂	21	55.7	74	74	143	111	87	—
121	♀	17	56.7	82	109	139	135	124	—
122	♂	39	63.6	93	83	109	127	116	—
123	♀	16	54.0	85	85	121	100	91	—
124	♂	73	54.5	96	100	143	95	95	Trace
125	♀	26	50.8	74	93	121	80	...	—
126	♂	30	72.7	100	125	185	222	91	+
127	♂	15	54.2	82	99	152	143	114	0
128	♂	32	70.8	103	91	156	154	114	0
129	♀	13	41.7	61	112	145	125	128	0
130	♀	14	41.5	60	102	176	131	108	0
131	♀	12	39.5	57	98	200	109	92	—
132	♀	16	50.3	73	93	133	81	102	0
133	♂	31	59.0	43	93	173	195	93	4.28
134	♂	26	40.6	62	87	172	174	109	0
135	♂	20	64.4	94	87	144	118	112	Trace
136	♀	16	66.0	48	117	136	158	90	0
137	♀	13	40.0	60	87	143	162	106	Trace
138	♀	26	56.6	85	97	112	139	117	Trace
139	♀	17	52.0	78	84	120	91	—	—
140	♂	22	56.8	86	80	111	93	86	0

TABLE 4.—*Blood Sugar Curves of Twenty-Three Healthy Students*

Number	Sex	Weight, Kg.	Glucose Given, Gm.	Blood Sugar				Glucose in Urine, Gm.
				Fast	½ Hour	1 Hour	2 Hours	
1	♂	56.6	85	123	133	148	165	0.16
2	♂	63.5	95	128	239	132	138	0.14
3	♂	68.0	100	141	195	174	125	1.50
4	♂	54.4	79	111	147	175	145	0.29
5	♂	78.0	100	94	163	188	129	0.15
6	♂	74.4	112	101	100	100	100	0
7	♀	45.8	67	98	107	118	104	0
8	♂	52.6	82	79	88	95	90	0
9	♂	62.6	94	87	87	56	87	0
10	♂	54.4	82	99	133	78	80	0.05
11	♂	64.8	97	102	165	116	102	0
12	♂	61.2	92	110	133	119	100	0.13
13	♂	68.9	100	95	165	119	103	0.20
14	♂	54.4	79	92	118	129	113	0.60
15	♀	55.8	81	98	127	98	133	0.23
16	♂	55.8	81	97	136	91	91	0
17	♂	64.9	94	97	109	95	105	0
18	♂	65.3	95	109	126	118	109	0
19	♀	46.7	68	90	145	122	117	0.45
20	♀	54.4	79	92	122	126	122	0
21	♀	67.6	100	108	152	148	139	0.33
22	♂	70.8	102	91	195	155	94	0
23	♂	61.2	92	112	133	164	140	0.30

TABLE 5.—*Change in Classification of Curves on Repeated Trial*

Classification of Initial Curve	Number of Patients	Average Number of Curves	A Subsequent Curve		
			High	Flat	Normal
High	19	3.2	—	0	13
Flat	4	2.2	0	—	4
Normal	20	3.4	3	5	—
Total	43	3.2	3	5	17

high curves found, and if we assume that the results from all patients would be the same as for the forty-three that had repeated curves, we estimate that of the total 140 patients examined approximately 20 per cent presented an unanticipated high blood sugar curve. In approximately half of these (10 per cent of the total), curves were persistently high, and in half they were only temporarily high. If we look on epilepsy as a symptom, it is possible that the constant decreased ability to dispose of ingested glucose shown by members of the first group may be of some etiologic importance as regards the convulsions. Against this possibility is the fact that during fasting the height of sugar curves was increased and the frequency of convulsions decreased. It would seem more probable that these few patients are potentially diabetic. It is possible that some of these patients, in the past having been interdicted from eating meat, had overtaxed their sugar burning mechanism by a high carbohydrate diet.

Joslin states that nearly 1 per cent of the population have diabetes. Of the 275 patients with epilepsy whose blood sugar we have measured, only two were diabetic. Forrer[37] reports that of the last 466 persons admitted to the Monson State Hospital, two, or 0.4 per cent showed glycosuria. This figure may be compared with 3 per cent, the proportion of patients with glycosuria coming to the male medical outpatient department of the Massachusetts General Hospital.[38] Because approximately 10 per cent of our epileptic patients presented a high blood sugar curve, where the statistics mentioned would suggest that the coexistence of diabetes and epilepsy is relatively uncommon, it is evident that only a small proportion of persons with a prediabetic type of blood sugar curve later develop diabetes.

FLAT CURVES

Long, low curves have been stated to occur in cretinism, progressive muscular dystrophy, hypopituitarism, and after thyroidectomy.[16] Table 2 presents the group of eight patients in whom flat curves were found. Of special interest are the inverted curves. In these patients, thirty minutes after the administration of glucose, blood sugar was below the prefasting value, following which it gradually rose to normal. Each of four patients with initial flat curves showed a normal curve on subsequent trial. Also five patients whose initial curves were normal later presented a flat curve. These are included in figure 3. In many of these patients, measurements of the basal metabolic rate proved to be within normal limits.

A possible explanation of the failure of the blood sugar to increase in these cases is lack of absorption of the sugar from the intestinal

37. Forrer, L.: Personal communication to the authors.

38. Lennox, W. G.: Temperature and Pulse Rates of Patients in Peking and Boston, China M. J. **66**:521 (March) 1925.

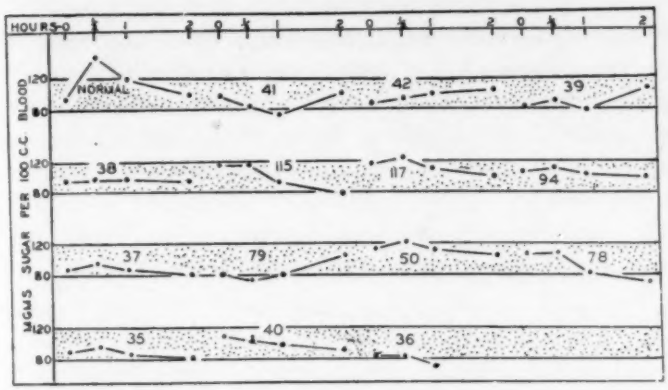

Fig. 3.—Abnormally low blood sugar curves in patients with epilepsy. Six of the curves are not initial curves.

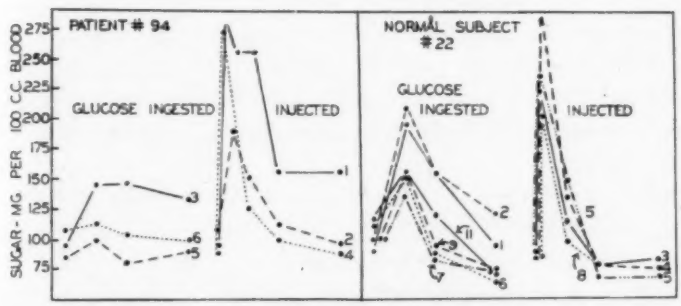

Fig. 4.—Six curves of patient 94 in contrast with ten curves of healthy subject 22. The curves of the latter are much more uniform. The amount of glucose ingested was five times the amount injected. In curves following injection of glucose, the first blood was taken at four minutes. In both methods, the first blood was taken with the patient fasting and, subsequently, one-half, one and two hours after the administration of the glucose.

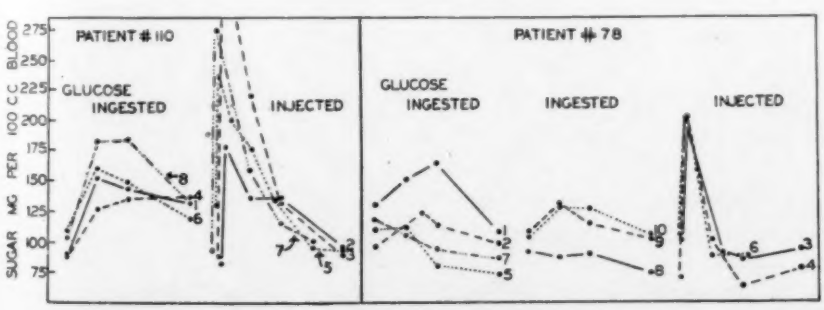

Fig. 5.—Eight curves of patient 110 and ten curves of patient 78, showing variation in the form of successive curves.

tract. We found, however, that several of our patients with flat sugar curves following ingestion of glucose also showed unusually rapid disappearance of glucose when it was injected intravenously.

That fact that a large proportion of students examined—four out of twenty-three—showed similar flat curves would tend to minimize their importance in this group of patients (table 4).

NORMAL CURVES

Table 3 shows the group of patients who fall in neither group 1 nor group 2. Although classified as normal, some of the curves are peculiar in shape. Seven of them rose to a peak of 180 mg. or more during the test, the so-called lag or steeple curve. One of these, no. 122, is shown in figure 1. Of twenty patients with normal initial curves who had repetition of the test, a subsequent curve was high in three and flat in five (table 5).

FREQUENTLY REPEATED CURVES

Various authors have stated that the general shape and level of the sugar curve of a healthy person, if done from time to time, remains fairly constant. This was true for a number of our patients. Some, however, showed considerable variation in both shape and level of successive curves.

Figure 4 shows ten curves of one of us, in comparison with six curves of patient 94. Successive curves of the healthy person, although assuming a lower level, are remarkably constant in form. The first curve of the patient, to whom glucose was given intravenously, is definitely diabetic in type. Subsequent curves differ greatly in form. This patient gave evidence of instability of the sympathetic system. On the occasion of making curve 6, the systolic blood pressure, while the patient was lying down, was 144. On standing, it was 120, but fell rapidly to 80, at which point the patient had to lie down because of faintness.

The evidence is complicated still farther because of the variability shown with the two methods of performing the blood sugar test. In figure 5 it may be seen that patient 110 had curves that were fairly constant in form when glucose was ingested, but differed greatly when glucose was injected. In contrast, the three intravenous curves of patient 78 are almost superimposed on one another, whereas the curves following ingestion of glucose vary in both level and form. This matter is discussed in more detail elsewhere.[39]

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39. Lennox, W. G., and Bellinger, M.: Comparison of Blood Sugar Curves Following Ingestion and Intravenous Injection of Glucose, Arch. Int. Med. **40**:182 (Aug.) 1927.

Figure 6 represents thirteen curves drawn at intervals during a period of two and one-half years on epileptic patient 79. Some of these are normal, some flat and some inverted. The variability was present both when sugar was given by mouth and when injected intravenously. There was no evident corresponding variation in the patient's physical condition, diet or manner of life. The seizures were light and infrequent. Though the body structure suggested disturbance of the pituitary gland, the sella turcica was normal in appearance, and roentgenographically. The basal metabolic rate was within normal limits—minus 7 per cent on two occasions.

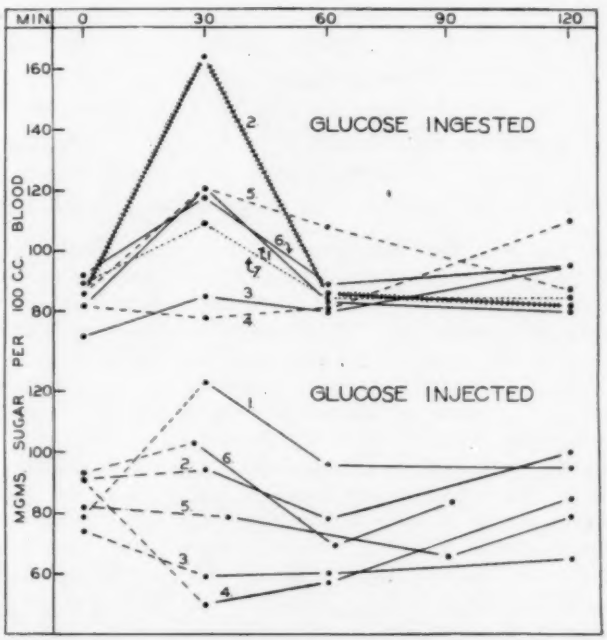

Fig. 6.—Twelve consecutive blood sugar curves in patient 79. In the fifth intravenous curve, double the usual dose was given.

Table 5 gives data concerning the forty-three patients in whom repeated curves following ingestion of sugar were done. In twenty-five of these (60 per cent) a subsequent curve differs in classification from the initial curve. We do not know how abnormal this variability is, because we have seen no observations concerning frequently repeated curves in healthy persons. Though for this reason a definite statement is impossible, we are inclined to believe that the degree of variability shown by certain patients was abnormally great, and may be an expression of coincident variability in the function of the sympathetic system with consequent changes in blood flow or in the activity of

endocrine glands. The fact that some of our patients who showed marked evidence of vasomotor disturbance had perfectly normal sugar curves prevents us from stressing this point.

It will be noted in table 5 and also in some of the figures that, of a series of curves, the later ones tend to become more normal. Whether this is due to decrease in the psychic reaction to the test, to a better regulated output of insulin in response to repeated administration of glucose, or to improved physical condition of patients under treatment, we have no means of judging. We deal with this question elsewhere.[40]

RELATION OF BLOOD SUGAR LEVEL TO SEIZURES

We have discussed this question in a previous paper, but have new evidence to present here. On several occasions a patient had a seizure while a glucose curve test was being performed, without apparent effect on the shape of the curve, nor did the level of blood sugar seem to influence the liability to seizures.

Marked changes of blood sugar were observed but bore no causal relation to seizures. Two interesting examples are the following:

Patient 137 had from 50 to 100 seizures of a myoclonic nature very day. At the end of a period of induced ketosis, during which she was entirely free of spells, she was given glucose by mouth for a sugar curve test. Fasting blood sugar and the curve were normal. Eight hours later seizures recurred, accompanied by a condition of tetany. Blood sugar at this time was 43 mg. It has been shown that hypoglycemia accompanies the tetany that follows extirpation of the parathyroids[41] and injection of guanidine.[42] With this observation, however, Collip[43] does not agree.

Patient 34, with severe diabetes, had his first convulsion following an overdose of insulin. The induction of hypoglycemia resulted on one occasion in a convulsion and on another occasion in unconsciousness. As the diabetes improved the convulsions became worse and occurred without reference to the administration of insulin. Detailed observations concerning this patient will be presented elsewhere.

RENAL THRESHOLD

In table 6, we have tabulated the proportion of patients who showed sugar in the urine following the ingestion of glucose. Of the 209 observations, glycosuria occurred in 32 per cent. Judged by this test—the one used before measurement of blood sugar was possible—a third

40. Lennox, W. G., and Bellinger, M.: Repeated Blood Sugar Curves in Nondiabetic Subjects, J. Clin. Investigation, to be published. Stimulation of the Sugar Regulating Mechanism as Shown by Duplicate Blood Sugar Curves, J. Biol. Chem. **73**:237 (May) 1927.

41. Underhill, F. P., and Blatherwick, N. R.: The Influence of Thyreoparathyroidectomy Upon the Sugar Content of the Blood and the Glycogen of the Liver, J. Biol. Chem. **18**:7, 1914.

42. Watanabe, C. K.: Studies in the Metabolic Changes Induced by the Administration of Guanidine Bases, J. Biol. Chem. **36**:531 (Dec.) 1918.

43. Collip, J. B.: The Parathyroid Glands, Medicine **5**:1, 1926.

of the patients showed a low sugar tolerance. How poor a measure this gives of the height of blood sugar is shown by the last column of the table. In persons with normal kidneys, glycosuria is supposed to occur when blood sugar reaches a height of from 150 to 175 mg. In 44 per cent of the tests, glycosuria did not occur when blood sugar measured more than 175 mg., and in 21 per cent, glycosuria did occur with the blood sugar below 150 mg. Therefore, in 30 per cent of the tests in which blood sugar was distinctly above or below the usual renal threshold, examination of the urine for sugar did not yield the expected result. This variation in renal threshold for sugar is greater than the variation found by John [14] in a group of nondiabetic patients. He did not find glycosuria present when blood sugar exceeded 175 mg. in 27 per cent of his observations; glycosuria was present with blood sugar below 150 mg. in 18 per cent, and in 19 per cent in which the

TABLE 6.—*Renal Threshold for Sugar in Two Hundred and Nine Observations*

Height of Blood Sugar Curve, Mg. per 100 Cc.	Number of Observations	Glycosuria		Percentage Showing Glycosuria
		Not Present	Present	
200 and more	28	10	18	64
175–199	38	19	19	50
150–174	43	34	9	21
125–149	60	43	17	28
125 and less	40	36	4	10
Total	209	142	67	32

height of the blood sugar curve was not reflected in the urinary examination for glucose. In only a few instances did the amount of sugar excreted by our patients during the test exceed 2 Gm.

COMMENT

Thirteen years ago, Cuneo [44] found in the serum of epileptic persons a proto-albumose which he maintains is responsible for seizures. He now attempts to fit insulin into the convulsion-producing mechanism. He argues that glucose is necessary for the synthesis of normal serum albumin, and that in conditions of hypoglycemia, an albumose, which produces convulsions, appears in the blood. His evidence, so far presented,[45] consists of the reduction in blood sugar which follows injection of both proto-albumose and insulin; a certain resemblance of the two in physical appearance and chemical reactions, and the finding of low blood sugar values after epileptic convulsions in five instances. In another

44. Cuneo, G.: Ricerche biochimiche sulla funzione ureoprojitica e sulle alterazione del sangue nell'epilessia, Riv. sper. di freniat. **40**:37, 1914.

45. Cuneo, G.: Della proto albumosa e delle sue relazioni con le crisi epilettiche e con le crisi insulin iche, Arch. di path. e clin. med. **5**:22, 1926.

publication,[46] he states that blood sugar was found increased after convulsions and that diminution in the frequency of seizures occurred in a group of nineteen patients coincidently with daily subcutaneous injections of unnamed amounts of glucose. Encouraged by these considerations, Cuneo would place the responsibility for the seizures of epilepsy either on insulin or on his insulin-like proto-albumose. With reference to these arguments, the chemical nature of insulin, whether proteose or not, is yet unknown. The administration of various substances, other than insulin, notably the guanidine compound recently synthesized by Frank, Nothman and Wagner,[47] will cause hypoglycemia. Also, the change in the level of blood sugar after convulsions is probably the result of the muscular work involved in the seizure. Muskens,[48] like Cuneo, would put insulin reactions in the same class as epileptic seizures. Other writers are content to see in fluctuations in blood sugar only the passive expression of activity of suprarenal glands (Kersten [49]), or of the vegetative nervous system (Holmstrom [2]). There is no doubt that under unusual conditions, such as already narrated in the case of patients 117 and 34, marked decrease in the concentration of blood sugar may accompany convulsions. The regulation of the concentration of blood sugar is, however, concerned with so many interrelated factors—the activity of the pancreas, suprarenal, pituitary and thyroid glands; the osmotic, electrolytic and acid-base relations of the blood; speed of blood flow and severity of muscular exertion; the condition of the liver, the kidneys and the gastro-intestinal tract and the general state of nutrition—that it is difficult to prove that a single factor is responsible for any changes that may be observed in the sugar level with relation to seizures.

Our observations (presented in this and a preceding paper [1]), based on approximately 2,000 measurements of blood sugar in 275 epileptic patients, fail to show any abnormality in carbohydrate metabolism (as measured by the concentration of sugar in the blood) which might be thought of as actively inducing seizures. We look on the few patients who present constantly high blood sugar curves as potentially diabetic, without any relation between that condition and the seizures. There is a larger group of patients who have sugar curves that are high only on initial trial (or that vary greatly from time to time) or who show

46. Cuneo, G.: L'azione convulsivante ed i cuoi fattori patogenetici, Riv. Sper. di freniat. **49**:65, 1925.

47. Frank, E.; Northman, M., and Wagner, A.: Ueber synthetisch dargestellte Körper mit insulinartiger Wirkung auf den normalen und diabetischen Organismus, Klin. Wchnschr. **5**:2100, 1926.

48. Muskens, L. J. J.: Epilepsie, Berlin, Julius Springer, 1926, p. 250.

49. Kersten, H.: Ergebunisse zur Frage des elementaren Krampfes Ztschr. f. d. ges. Neurol. u. Psychiat. **63**:48, 1921.

abnormal fluctuation of the renal threshold for sugar. We think of these patients as presenting an instability of the sugar disposing mechanism, which is the reflection of an underlying instability of physiologic function. Whether this is concerned principally with the glands of internal secretion, with the sympathetic nervous system, with the acid-base balance of the body, or with something else we can only speculate.

CONCLUSIONS

1. Study of the carbohydrate metabolism in 140 epileptic patients has been made by means of 400 blood sugar curves.

2. Of the 140 initial curves 24 per cent were abnormally high, 6 per cent abnormally low, and 70 per cent within the normal range. About 10 per cent of the patients had high sugar curves which could not be accounted for by coincident disease conditions and which remained high on repeated examination. These patients probably represent potential diabetics.

3. A larger percentage showed marked variation in the form and level of successive sugar curves or abnormal fluctuations in the renal threshold for sugar. Possible causes of this instability of the sugar regulating mechanism are discussed.

4. The data collected gave no evidence of abnormality of carbohydrate metabolism that might in itself induce seizures.

SPASMODIC ASSOCIATED MOVEMENTS OF THE EYES

CAN THEY BE PRODUCED BY SYPHILIS? *

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Spasmodic associated movements of the eyeballs, during which the eyes are drawn laterally, upward or downward and are fixed for varying periods of time in that position, have been observed recently in a number of cases of epidemic encephalitis of the parkinsonian type. The first series of cases was reported by Fischer,[1] in 1924. He studied five patients in whom the eyes were drawn upward, or to one side and upward. On the basis of the results obtained by functional vestibular tests, normal during the aspasmodic phase, the spasm being increased during the period of deviation, he concluded that the lesion producing this symptom was situated in the same locality as that producing the concomitant disturbances of the skeletal musculature, i. e., the corpora striata. Meyer [2] reported two cases, in one of which the eyes were drawn to the left and downward, and in the other, upward. On account of the association of the spasmodic deviation with forced laughing and crying, he placed the lesion in the thalamostriate complex. Ewald [3] reported five cases; in two, the deviation was to one side and in three, upward. In his opinion, the spasm was caused by periodic irritation or arrest of inhibition of the structures in the region of the corpora quadrigemina. Lemos [4] reported one case in which the head and eyes were turned to one side. In this case there were also cramps during writing and intermittent claudication and spasms of the muscles of mastication, of the tongue, palate and larynx, and of the upper limbs. He considered that these phenomena were the result of a localized lesion of the corpora striata, with an extension into the internal capsule involving the oculogyric and cephalogyric pathways. Hohman [5] reported four cases, in all of which the eyes were drawn upward. He considered this to be symptomatic of an active focus of inflammation in the mid-

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1. Fischer, Bruno: Deutsche Ztschr. f. Nervenh. **81**:164, 1924.
2. Meyer, A.: Arch. f. Psychiat. u. Nervenh. **70**:466, 1923-1924.
3. Ewald: Monatschr. f. Psychiat. u. Neurol. **57**:222, 1924.
4. Lemos, M.: Rev. neurol. **2**:425 (Nov.) 1924.
5. Hohman, L. B.: Forced Upward Conjugate Movements of Eyes in Post-encephalitic Parkinson's Syndrome, J. A. M. A. **84**:1489 (May 16) 1925.

brain. Marinesco, Radovic and Draganesco [6] observed five cases. In two, the deviation was lateral and in three, to one side and upward. Their results with functional vestibular tests agreed with those of Fischer. They concluded that the lesion responsible for these attacks was situated in the extrapyramidal system and liberated tonic centers in the pallidum, the attacks obeying the same laws that govern convulsive seizures of cortical origin. Popowa [7] reported five cases. In two patients the eyes were drawn upward, in two to one side and downward, and in the fifth, downward. She placed the lesion in the corpora striata. Beriel and Bourrat [8] reported three cases; in two, the eyes deviated upward and to one side, and in the other, upward. In these three patients, the attacks were accompanied by palpebral spasm. Pappenheim [9] observed three cases, in all of which the eyes were turned upward. Schwartz and Bing [10] reported three cases and attributed the attacks to a lesion of the supranuclear tracts, as the spasms resembled supranuclear epilepsy. Kulkow [11] reported the case of a young man, with deviation of the eyes to the left and concomitant inability to close the eyelids. During these attacks the arms were held strongly adducted and flexed, and the patient could not answer questions. Pupillary reactions to light and in convergence were absent. Kulkow does not hazard a theory as to the localization of the lesion but stresses the inability to produce willed movements during the attack, although the eyes moved passively when fixed on a stationary point and the head rotated. Barkas [12] observed three cases; in two the deviation was upward and to the left, and in the other upward. In her report she refers to another case observed by Mapother. Reports were made by three other authors [13] which were not available for this paper.

The comparative paucity of reports in the literature does not indicate the frequent occurrence of this symptom in encephalitic parkinsonism.

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6. Marinesco, G.; Radovici A., and Draganesco S.: Rev. neurol. **1**:148 (Feb.) 1925.

7. Popowa, Nina: Ztschr. f. d. ges Neurol. u. Psychiat. **97**:515 (July) 1925.

8. Beriel L., and Bourrat: Lyons méd. **136**:45, 1925.

9. Pappenheim, M.: Neurol., neuropath., psychol., psychiat. mém. publiés à l'occasion du jubilé du Prof. G. Rossolimo, Moscow, 1925, p. 602.

10. Bing & Schwartz: Encéphale **20**:150, 1925.

11. Kulkow, A. E.: Ztschr. f. d. ges Neurol. u. Psychiat. **102**:636 (June) 1926.

12. Barkas, M. A.: Lancet **2**:330 (Aug. 14) 1926.

13. Bakker, S. P.: Nederl. Tijdschr. v. Geneesk. **69**:2148, 1925, reported a case of ocular spasm with syphilitic infection resembling the shaking palsy; Benton, G. H.: J. Florida M. A. **12**:12 (July) 1925, reported a case of a post-encephalitic syndrome with potent conjugate upward movement of the eyes with temporary fixation; Giraud, G.: Rev. d'oto-neuro-ocul., 1925, p. 705, reported a case of tonic vertical oculogyric crises with spasm of the eyelids in a patient with postencephalitic parkinsonism.

All the cases reported to date have been observed clinically and not any patient has been examined pathologically, so that one can only speculate as to the location of the causative lesion. Most of the authors quoted conclude that it is situated in the corpora striata. Muskens [14] has shown, on the basis of animal experimentation, that the vestibular mechanism, mediated through the posterior longitudinal bundle and the cerebellomesencephalic tracts, exercises a controlling influence on certain subsidiary centers in the midbrain, whose function is to produce associated movements of the eyes. These centers are: the nucleus of the posterior commissure for lateral movements; the nucleus interstitialis for "skew" movements; the juxtarapheic portion of the tegmentum of the midbrain, ventral to the posterior longitudinal bundle, for upward movements, and a center situated ventrad to the last mentioned for downward movements. As in the cases under discussion the vestibular reflex mechanism is intact, as proved by the normal vestibular responses, the lesion must be placed at a higher anatomic level than these subsidiary centers, i. e., either in the corticonuclear tracts or in the extrapyramidal system.

It does not seem reasonable to believe that irritation of the corticonuclear pathway could continue over an extended period of time, such as has elapsed in these cases, without resulting eventually in interruption of the tract and cessation of function. Furthermore, if the symptom was produced by irritation one would expect it to appear early in the course of the disease, and in none of the reported and personally observed cases has it appeared earlier than one year after the development of the associated parkinsonian condition. A similar line of reasoning tends to refute the theory that irritation, either of the lower midbrain centers or of the corpora striata, is the causative factor, for, though it is well known that active lesions of encephalitis are present even years after the inception of the disease, it would seem strange that these irritative lesions would not produce the symptom earlier in the life history of the condition.

Paralyses of vertical and lateral gaze, which occurred previous to the epidemic of encephalitis, are well known to be caused by lesions of the lower portions of the efferent and reflex pathways, as Spiller [15] and, more recently, Freeman [16] have shown. Epidemic encephalitis has produced a similar condition due to lesions of the corpora striata and midbrain, but in none of these cases has there been found the peculiar spasmodic deviations that have been reported recently, as would be expected in accordance with the law that irritation precedes paralysis.

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14. Muskens, L. J. J.: Brain **36**:352, 1914; **45**:454, 1922.

15. Spiller, W. G.: J. Nerv. & Ment. Dis. **32**:417 (July) 1905.

16. Freeman, W.: Paralysis of Associated Lateral Movements of the Eyes, Arch. Neurol. & Psychiat. **7**:454 (April) 1922.

If these deviations are not produced by irritative lesions, they must be caused by the release of the activity of a lower level (in the sense of Hughlings Jackson) following the destruction of a higher. This release of function occurs, as Hunt [17] and others have pointed out, in the production of choreo-athetoid movements by disease of the neostriatum. The spasmodic associated movements of the eyes have a resemblance to movements of the choreo-athetoid type and it seems probable that, if the various motion formulas have a representation in the striatal complex analogous to their representation in the cortex (and the work of Karplus and Kreidl [18] as to a pupillodilator center in the hypothalamic region points strongly to this assumption, at least for movements of the eye) these spasmodic deviations are caused by the release of these centers from their neostriatal control. This seems further to be borne out by the fact that, in long continued encephalitis, two types of lesions are found, an acute inflammatory round cell infiltration and a progressive degeneration of ganglion cells. This progressive degeneration, occurring as the result of previous inflammatory changes, would explain also the late appearance of this symptom.

If the anatomic location of the lesion occurs as was suggested and if, in the large number of reported cases, encephalitis is the etiologic factor, can a disease process of a similar pathologic nature, situated in this locality, produce this symptom? A search of the literature reveals four clinical causes in which a symptom somewhat analogous to that reported here occurred previous to the epidemic of encephalitis. Nothnagel [19] reported the case of a man who sustained a severe injury to the head which was followed by the development of choreo-athetoid movements of the hand. When he attempted to look upward he could not lower the eyes again for some time, but they were held in the upward position by a strong spasm. Kunns [20] described the case of a man, aged 43, who had suffered since childhood from weakness and athetosis of the right arm. He developed spasms of the muscles of mastication and of the pharynx, distortion of the mouth and protrusion of the tongue to the right. When he started to go to sleep or on waking, he suffered from a spasmodic movement of the eyes, upward and to the right, at first only when he tried to look upward, and later if he were frightened. Schröder [21] reported the case of a man, aged 31, who was attacked suddenly by high fever, headache, vomiting and convulsions, accompanied by complete ophthalmoplegia and extensive

17. Hunt, J. R.: Am. J. M. Sc. **162**:481, 1921.

18. Karplus and Kreidl: Arch. f. d. ges. Physiol. **129**:338, 1909; **135**:401, 1910; **143**:109, 1912.

19. Nothnagel: Wien. med. Bl., 1884, p. 575.

20. Kunns: Deutsche med. Wchnschr., 1897, p. 370.

21. Schröder: Quoted by Marie (footnote 22).

amblyopia. These symptoms disappeared after four or five weeks, but he was left with paralysis of associated movements of the eyes. When he attempted to look downward, spasmodic associated movements upward occurred. A case of spasmodic associated movements of the eyes upward was presented by Marie [22] before the Paris Neurological Society. The opinions of those who discussed the case diverged markedly as to whether the condition was functional or organic, but from a careful perusal of the case report, it seems necessary to conclude, with Spiller,[15] that there was more to substantiate an organic than an hysterical etiology. Neither in this case nor in that of Kunns is the etiologic factor reported.

The following case of spasmodic associated movements of the eyes upward, in a patient with a parkinsonian symptom complex, is reported because of the concomitant occurrence of a positive Wassermann reaction in the blood, which at once raised the question whether the whole syndrome might not be caused by syphilis rather than by encephalitis.

REPORT OF CASE

Clinical History.—G. B., a colored woman, aged 20, was referred to the neuropsychiatric clinic of the Pennsylvania Hospital from the clinic for syphilis. The family history is unimportant. As a child, the patient suffered from measles, mumps and whooping cough. At the age of 12 she had an attack of malaria. In 1918, she was confined to bed for two weeks by an illness that was diagnosed as influenza; she had general malaise and fever, but no lethargy, diplopia, ptosis, or other symptom that would suggest encephalitis. In 1921, she noticed that the right hand was becoming weak and was beginning to tremble. This weakness and tremor increased, spreading to the arm and the right leg; for the past one and a half years this has remained stationary. In 1923, she commenced to have attacks of spasmodic movements of the eyes. In these attacks the eyes were drawn strongly upward, and she was unable to move them in any direction while the spasm lasted. Accompanying the spasm was a sense of discomfort in the eyeballs. The attacks occurred about every two or three days and usually lasted ten minutes. Recently, accompanying the attacks, she had had a feeling that the eyes were being drawn into a convergent position. For the last year she had suffered from diplopia, the false image being to the right of the true.

Physical Examination.—The patient was thin and had a slight degree of "mask" facies. The right arm was held rigidly, the elbow being flexed and the hand pronated. On walking, the right arm did not swing, the right leg was dragged at each step, and the gait somewhat resembled that of hemiplegia. The ocular rotations were full in all directions; the pupils were equal and regular; the reaction to distance was normal; the reaction of the right pupil to light was limited in extent and what little movement there was took place slowly. The fundi were normal. Wrinkling of the brow and closing of the eyes was done equally well on both sides. The lower part of the face on the right was flatter than on the left, and movement on that side was of less extent and

22. Marie, P.: Rev. neurol. **9**:428, 1901.

weaker. The tongue was protruded straight, but on protrusion showed a fine tremor. The grasp of the right hand was weak, as were all movements of that extremity, except those of the shoulder girdle. There was moderate rigidity of the right arm to passive motion. The reflexes there were increased. There was continuous tremor of the whole arm, fine in character and altered little, if at all, by movement. This tremor was most pronounced in the hand, imparting a pill rolling motion to the thumb and index finger. The right abdominal reflexes were absent. The right leg showed a condition similar to that in the right arm, with rigidity, tremor, weakness and increased reflexes. The plantar reflex on that side was of flexor type and no clonus was found. The left arm and leg were normal. Sensation for touch, prick, heat, cold, two-point discrimination, position and vibration were normal everywhere. The finger-to-nose and heel-to-knee tests were poorly done on the right on account of the tremor. Signs of cerebellar involvement were not present.

The general physical condition did not show any abnormalities, except slightly enlarged and cryptic tonsils and palpable cervical glands. The blood was strongly positive to the Wassermann test. The cerebrospinal fluid was under pressure of 14 mm. of mercury; there were three cells, a faint trace of globulin and the Wassermann reaction was negative. A colloidal gold test was not done.

Course.—During the first three weeks she was under observation, the patient had seven attacks of upward spasmodic deviation of the eyes.

This case merits consideration for two reasons. Can associated spasmodic movements of the eyes be produced by any etiologic factor other than encephalitis and, more important from the patient's standpoint, can syphilis produce it? In the latter case, treatment may produce considerable amelioration of symptoms, and the outlook is not as hopeless as in encephalitis of the epidemic type. From this aspect, differential diagnosis intra vitam is of manifest importance and I have reviewed the literature from the standpoint of the parkinsonism, as it is linked undoubtedly with the movements of the eyes and as the literature on the latter is so scanty, to determine whether there are criteria by which such a diagnosis may be made.

SYPHILIS AS A CAUSATIVE FACTOR

That syphilis may be the etiologic factor for the production of a certain number of cases of parkinsonism seems attested by the comparatively large number of case reports in the literature. In considering these cases, it seems necessary to make a distinction between idiopathic paralysis agitans and syphilitic parkinsonism on the one hand, and between the latter and postencephalitic paralysis agitans on the other. This distinction may be made best from the manner of onset, the course of the disease and the age at which the onset occurs. The latter is of manifest importance in that the idiopathic form is well known to be of rare occurrence before 45 years of age, and the postencephalitic form occurs most commonly in younger persons. (This distinction on the basis of age is not adhered to in the cases of tabes and general

paralysis associated with parkinsonism, which are all included in the first group.) The differential diagnosis of the first group does not concern the question raised regarding my patient, but it is thought wise to include it for reasons that will become manifest later.

In regard to this group—the patients of 45 years and over—I have been able to find twenty cases, in which the diagnosis was verified at necropsy. The seven cases of Ewald,[23] Knessner,[24] Krabbe,[25] Urechia,[26] Wimmer,[27] Urechia and Elekes (case 4)[28] and Mella and Katz,[29] were of general paralysis, in which the parkinsonian syndrome developed as a late manifestation. Two of these cases, those of Urechia and Elekes (case 4) and of Mella and Katz, were clinically the tabetic type of general paralysis. One patient, case 2 of Urechia and Elekes, showed the clinical signs of tabes.

Psychic manifestations, such as dementia, feeble memory, apathy and depression with suicidal attempts, occurred in eight cases, those of Westphal,[30] Lhermitte (cases 1, 2, 3 and 5),[31] Urechia, Michalescu and Elekes (case 1),[32] Pette [33] and Urechia and Elekes (case 2).[28]

Eight patients showed signs of disease of the pyramidal tract in association with the extrapyramidal syndrome—those of Loeper and Torestier,[34] Lhermitte (cases 1, 4 and 5),[31] Urechia, Michalescu and Elekes (case 2),[32] Wimmer,[27] Pette,[33] and Urechia and Elekes (case 1).[28]

Four cases showed clinical signs of systemic syphilis, such as aortitis, choroiditis, etc.—those of Urechia,[26] Urechia and Elekes (cases 1 and 3),[28] and Mella and Katz.[29] In the last case, there was also a definite history of syphilis.

Seven patients, those of Loeper and Forestier,[34] Urechia and Elekes (case 2),[28] Lhermitte (cases 2, 3, 4 and 5),[31] and Mella and Katz,[29] suffered from incontinence. Four of the five patients reported by Lhermitte [31] suffered from dysphagia and dysarthria.

Argyll Robertson pupils were present in nine patients—those of Ewald,[23] Westphal,[30] Urechia,[26] Urechia and Elekes (four cases),[28]

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23. Ewald: Deutsche Arch. f. klin. Med. **19**:591, 1877.
24. Knessner: Arch. f. Psychiat. **8**:443, 1878.
25. Krabbe, K.: Ztschr. f. d. ges. Neurol. u. Psychiat. **9**:571, 1912.
26. Urechia, C. I.: Rev. neurol. **37**:584, 1921.
27. Wimmer, A.: Rev. neurol. **38**:38, 1922.
28. Urechia and Elekes: Encéphale **18**:503, 1923.
29. Mella, H., and Katz, S. E.: J. Nerv. & Ment. Dis. **59**:225 (March) 1924.
30. Westphal: Arch. f. Psychiat. **60**:361, 1919.
31. Lhermitte, J.: Rev. neurol. **38**:406, 1922.
32. Urechia, Michalescu and Elekes, quoted by Urechia and Elekes (footnote 28).
33. Pette, M.: Deutsche Ztschr. f. Nervenh. **77**:256, 1923.
34. Loeper, M., and Forestier, J.: Bull. et mém. Soc. méd. d. hôp. de Paris **45**:226 (Feb. 18) 1921.

Lhermitte (case 1),[31] and Mella and Katz.[29] In Wimmer's case the light reflex was sluggish, and in Knessner's patient the pupils were unequal.

OTHER SIGNS OF INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM

The accompanying table illustrates the serologic observations in the cases reported since the Wassermann test came into general use.

In every one of these cases there are signs that point to involvement of parts of the central nervous system other than the extrapyramidal complex. Signs of general paralysis, tabes, disease of the pyramidal tract, mental symptoms, pupillary abnormalities or signs of systemic syphilis could be demonstrated clinically. The question at once arises: Do these complicating signs occur in cases of idiopathic

*Wassermann Reactions in Recorded Cases**

Author	Blood	Spinal Fluid
Krabbe	Positive	
Westphal	Positive	Negative
Urechia	Positive	Positive
Wimmer	Negative	Negative
Urechia et al:		
Case 1		Positive
Case 2	Negative	Negative
Urechia and Elekes:		
Case 1	Positive	Positive
Case 2	Negative	Negative
Case 3	Positive	Positive
Case 4	Positive	Positive
Mella and Katz	Positive	Negative
Lhermitte:		
Case 3	Positive	
Case 5	Positive	
Pette	Positive	Positive
Loeper and Forestier	Negative	Negative
De Massary	Positive	Positive
Pappenheim		Positive

* It is well known that the results of the serologic tests are usually negative in idiopathic paralysis agitans. Through the kindness of Dr. N. W. Winkelman of the Neuropathological Laboratory, Philadelphia General Hospital, all cases of uncomplicated paralysis agitans from which autopsy material was available were studied from this standpoint and in only one was a positive blood Wassermann reaction found. This case illustrates the fallacy of placing too much dependence on a positive result, for the pathologic examination did not show any syphilitic lesions, either in the nervous system or in other organs.

paralysis agitans? The cases showing the symptom-complex of general paralysis and tabes may be excluded from this discussion, as in such definitely specific conditions, the syphilitic etiology of the parkinsonism must be taken for granted.

In seven of the cases that showed psychic manifestations, the mental symptoms were associated with other complications, Argyll Robertson pupils, pyramidal tract signs, etc. In the case of Urechia, Michalescu and Elekes, death occurred at 59, an age when senile mental changes may develop, though rarely. The mentality is usually well preserved in paralysis agitans until long after this time of life.

Cases with signs of disease of the pyramidal tract, either in the form of hemiplegias or pseudobulbar paralytic syndromes, form the most

difficult group in which to make a clinical diagnosis of syphilitic parkinsonism. In three of the reported cases, Argyll Robertson pupils were present—those of Lhermitte (case 1), Wimmer, and Urechia and Elekes (case 1). In the last case, concomitant signs of systemic syphilis were also present. In the remaining five, there is no symptom group that will enable one to distinguish them from the pyramidopallidal syndromes of later life, etiologically nonspecific, especially as Lhermitte and McAlpine [35] recently have reported a case and erected a pyramidopallidal symptom complex which is not the result of syphilis. In these cases, though one immediately perceives that the condition is not a true parkinsonism, it is perhaps necessary to rely on the serologic studies, though, as the accompanying table shows, these may give negative results also. Incontinence, while serving to indicate that the patient probably is not suffering from a true idiopathic paralysis agitans, in itself does not aid in distinguishing a specific etiology.

Among the clinical cases reported by Reuter,[36] Maillard,[37] Marchand and Petit,[38] Regis,[39] Mirallie,[40] Stertz,[41] Spatz (two cases),[42] the parkinsonism was incidental to the course of general paralysis. Twenty cases, those of Heimann (two cases,[43] Placzek,[44] Weil,[45] Hess,[46] Wertheim-Salomonson,[47] Daddi,[48] Rhein (three cases),[49] Bychowski,[50] Bruns,[51] Eshner,[52] Camp,[53] De Massary,[54] Wilson and Cobb (four cases)[55] and Gibson [56] were of associated tabes and paralysis agitans. Pette [33] quotes

35. Lhermitte, J., and McAlpine, D.: Brain **49**:157 (June) 1926.
36. Reuter, C.: Orvosi hetil., 1904, no. 7; abstr. in Neurol. Centralbl. **23**:375, 1904.
37. Maillard, G.: Rev. neurol. **20**:674, 1910.
38. Marchand and Petit, quoted by Urechia and Elekes (footnote 28).
39. Regis, quoted by Urechia and Elekes (footnote 28).
40. Mirallie, C.: Ztschr. f. d. ges Neurol. u. Psychiat. **11**:614, 1912.
41. Stertz, C.: Abhandl. a. d. Neurol., Psychiat., Psychol. und ihren Grenzgebieten, 1921, part 11, p. 1.
42. Spatz, H., quoted by Urechia and Elekes (footnote 28).
43. Heimann: Graduation Thesis, Berlin, 1888.
44. Plazek: Deutsche med. Wchnschr., 1892, p. 632.
45. Weil: Neurol. Centralbl. **17**:713, 1898.
46. Hess: Neurol. Centralbl. **19**:583, 1900.
47. Wertheim-Salomonson: Neurol. Centralbl. **19**:741, 1900.
48. Daddi: Riv. crit. de clin. méd. **4**:145, 1903.
49. Rhein, J. H.: Three Cases of Involuntary Movements in Locomotor Ataxia, J. A. M. A. **39**:1632 (Dec. 27) 1902.
50. Bychowski: Neurol. Centralbl. **23**:786, 1904.
51. Bruns: Neurol. Centralbl. **23**:978, 1904.
52. Eshner: Am. J. M. Sc. **138**:729, 1909.
53. Camp, C. D.: J. Nerv. & Ment. Dis. **41**:489 (Aug.) 1914.
54. De Massary: Rev. neurol. **38**:1368, 1922.
55. Wilson, S. A. K., and Cobb, S.: J. Neurol. & Psychopath. **5**:44 (May) 1924.
56. Gibson, E. T.: M. Clin. N. Amer. **7**:1303 (Jan.) 1924.

Seiffer, Karplus and Bonheim as reporting similar cases. Seven of the other clinical cases fall within the life period of paralysis agitans. In Ranmer's patient [57] there were pupillary signs of syphilis, as was also true of Pette's patient. The cases of Urechia,[26] Coppola,[58] and Achard and Rouillard [59] present indefinite signs of disease of the pyramidal tract, complicated in the first two instances by pains of a tabetic character and in the first and last cases by pupillary disturbances. These two patients were improved by antisyphilitic treatment, as were the patients mentioned by Pette, O. Foerster [60] and E. Forster.[61]

If it is possible to distinguish syphilitic parkinsonism from idiopathic paralysis agitans on the basis of the concomitant occurrence of signs extraneous to those due to extrapyramidal disease, it remains then to determine whether, in the younger group of patients, 45 years and under, it is possible to distinguish between a parkinsonian syndrome due to syphilis and one due to other causes, notably epidemic encephalitis. Of the sixteen case reports of syphilitic parkinsonism occurring in this age group, only two have been studied pathologically. In 1922, De Massary [54] reported the case of a woman, aged 42, who was ill for three months with an attack of influenza, during which, in addition to fever and pains in the arms, lethargy was present. A year later she developed a typical parkinsonian syndrome and six months after this appeared, a cutaneous eruption was noticed, which was diagnosed as syphilitic. The Wassermann reactions with the blood and spinal fluid were both positive. At autopsy, a mild perivascular infiltration was found in the region of the basal ganglia. From the case report, it seems reasonable to suppose that originally this patient suffered from encephalitis and that the syphilitic infection was concomitant only and not causative of the parkinsonism.

A similar association of the two diseases occurred in the other case, that reported by Pappenheim.[62] A man, aged 41, suffered from a typical attack of acute epidemic encephalitis in 1921. Two years later he developed the Parkinson syndrome. The pupils were normal, but the left ankle reflex was diminished and the right was absent. The man complained of sharp, shooting pains in the right leg. The cerebrospinal fluid showed 60 cells, increased globulin content, a positive Wassermann reaction and a meningovascular curve in the colloidal gold test. At necropsy, marked inflammatory changes in the meninges and

57. Ranmer, quoted by Urechia and Elekes (footnote 28).

58. Coppola, A.: Riv. di patol. nerv. **27**:99, 1922.

59. Achard, C., and Rouillard, J.: Bull. et mém. Soc. méd. d. hôp. de Paris **45**:130 (Nov. 2) 1921.

60. Foerster, O.: Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:1, 1921.

61. Forster, E., quoted by Foerster (footnote 60).

62. Pappenheim, M.: Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:81, 1925.

parenchyma were found. The majority of the cells of the pallidum were intact, but the substantia nigra showed marked alterations. The lower part of the spinal cord showed involvement of the root entry zone of the posterior root and degeneration of the posterior columns. The author concluded that the tabetic symptoms were caused by syphilis and the alteration in the basal ganglia by encephalitis.

ETIOLOGY OF EXTRAPYRAMIDAL DISEASE

The clinical cases reported are indefinite in establishing the specific etiology of extrapyramidal disease. In Tinel's [63] case the etiology was supposed to be traumatic excitation of a syphilitic process, but the diagnosis rested solely on the improvement under treatment, the relapse when treatment was stopped and reimprovement under further treatment. Pette's patient [33] had paralysis agitans sine agitante and positive serologic tests; he also showed some improvement following specific therapy. In Wimmer's case,[27] the diagnosis rests entirely on the positive serologic tests. The case reported by Schaeffer and Boulanger [64] began acutely with delirium, diplopia and pain in the left leg. Before the parkinsonism developed, the spinal fluid was normal. When the paralysis agitans syndrome was full blown, there were unequal pupils, lightning pains in the left leg, and a positive Wassermann reaction with the blood. The latter signs and the history of syphilis were the points on which the diagnosis was based. In Nordman and Cachet-Balnung's two cases,[65] the history, the presence of the lightning type of pains and the positive Wassermann reaction in both the blood and the spinal fluid were the diagnostic features. Halbron, Léri and Weismann-Netter's case [66] is one that probably seems syphilitic, despite the negative serologic examinations. This woman, aged 34, who had had four miscarriages and two dead infants, developed a Weber's syndrome, with right facial palsy and paralysis of gaze. The pupils were unequal; the right was miotic and the light reflex was absent. There was a parkinsonian tremor of one side. Demay and Petithory's case [67] began with depression at the age of 41, then somnolence and headache. There were pains in the arms and legs, muscular spasms and later a typical paralysis agitans sine agitante. At this time the knee reflexes were unequal; there was a doubtful Babinski sign, the pupils were miotic, irregular and reacted poorly to light. The Wassermann and colloidal benzoin tests were

63. Tinel, J.: Rev. neurol. **36**:878, 1920.

64. Schaeffer, H., and Boulanger, Petit: Rev. neurol. **38**:1365 (Nov. 9) 1922.

65. Nordman and Cachet-Balnung: Loire méd. **36**:351, 1922.

66. Halbron; Léri, A., and Weismann-Netter: Rev. neurol. **39**:547 (Aug. 11) 1923.

67. Demay, G., and Petithory, A.: Bull. de la Soc. clin. de méd. ment. **11**:303 (Dec.) 1923.

positive. Under specific treatment the symptoms improved a little. In Gibson's case [66] there was a history of syphilis, the pupils were unequal, the reaction to light was limited and the Wassermann, globulin and colloidal gold reactions with the spinal fluid were positive. The two case reports of Mella and Katz [29] contained histories of syphilis, but there were also vague histories that might be interpreted as acute attacks of encephalitis; the consensus of opinion was that they were postencephalitic and not syphilitic. In 1924, Gordon [68] formulated the following diagnostic points, which he concluded served to distinguish syphilis from encephalitis: the early appearance and persistence of diplopia, ptosis and the Argyll Robertson pupil, the absence of myoclonia, the marked degree of tremor and its early disappearance, the shortness of the somnolent period, involvement of the sphincters, mental dullness and absence of fever favor the diagnosis of syphilis. In his cases the diagnosis was made largely on the presence of the positive Wassermann reaction and the improvement occurring under treatment; perusal of his case histories does not tend to convince one of his differentiation.

With the exception of the case reported by Halbron, Léri and Weismann-Netter, none of these reports is convincing as to the syphilitic etiology; even their case, in the light of Pappenheim's, is not proved beyond a reasonable doubt. In two diseases with as similar a pathologic picture as encephalitis and syphilis, the clinical differentiation becomes difficult. All the signs relied on to distinguish idiopathic paralysis agitans and syphilitic parkinsonism—the state of the pupils, mental symptoms, pyramidal tract signs and incontinence—are valueless as they may occur in definitely nonsyphilitic encephalitis. Serologic results are also not diagnostic, as other authors as well as myself [69] have reported cases of asymptomatic neurosyphilis with positive serologic tests, both in the blood and the spinal fluid, in young patients, and any of these patients might contract epidemic encephalitis, later develop the parkinsonian syndrome, and be found on examination to have the same positive serologic characteristics. Neither is improvement under antisyphilitic treatment a sure criterion, for many cases of encephalitis improve under antisyphilitic therapy to a greater or less extent.

Paralysis agitans may be produced by the location of the lesions of syphilis in the region of the basal ganglia, but, though theoretically a similar location of specific lesions might produce symptoms simulating postencephalitic parkinsonism, there are no proved cases of the condition occurring in persons before the period of life at which idiopathic paralysis agitans develops, and in a given case there

68. Gordon, A.: J. Nerv. & Ment. Dis. **59**:251 (March) 1924.
69. Scott, G. O., and Pearson, G. H. J.: Am. J. Syph. **4**:201, 1920.

are no clinical criteria by which a diagnosis of syphilitic parkinsonism rather than postencephalitic parkinsonism may be made. Similarly, though a few cases of spasmodic associated deviations of the eyes have been reported as being the result of other etiologic factors than epidemic encephalitis, such as trauma, and though, theoretically, a syphilitic lesion liberating the lower extrapyramidal centers might produce it, I do not consider that in the case reported a diagnosis of syphilitic disease of the corpora striata can be made; all the evidence points to the etiologic factor being encephalitis of the epidemic type.

CONCLUSIONS

1. Spasmodic associated movements of the eyes are a frequent symptom in the cases of postencephalitic parkinsonism seen at present.

2. This symptom is probably a release phenomenon due to degeneration of the controlling centers in the neostriatum.

3. The same symptom perhaps may be due to other etiologic factors, but the reported cases are not conclusive.

4. The parkinsonian syndrome may occur in later life on a syphilitic basis and is distinguishable by the fact that there are signs denoting the involvement of other parts of the central nervous system which are not involved in idiopathic paralysis agitans.

5. It cannot be differentiated clinically from Lhermitte and McAlpine's pyramidopallidal syndrome.

6. No proved case has been reported of syphilitic parkinsonism occurring in the early half of life, all such cases really being caused by encephalitis, though the patient may have a concomitant syphilis.

7. There is no diagnostic sign whereby such cases, if they do occur, can be differentiated from those due to encephalitis.

Clinical and Occasional Notes

PAROXYSMAL SPASM OF THE EYELIDS AS A POST-ENCEPHALITIC MANIFESTATION*

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The pupils, the muscles of the eye, the eyelids and the optic disks are commonly involved in encephalitis, and within the past few years forced movements of the eyeballs have been observed as a fairly frequent sequel. While drooping of the eyelids, especially in the acute stages of the disease, due to paralysis of the oculomotor nerves, is a well recognized sign, less attention has been paid to paroxysmal spasm of the eyelids except by a few French authors. This is probably the result of the fact that spasm of the eyelids after encephalitis is a comparatively rare phenomenon and is infrequently observed. For this reason, attention is directed to this manifestation of encephalitis as exhibited in one case of our own and as observed in the few instances by others.

REPORT OF CASE

Paroxysmal spasm of the eyelids occurring as a late manifestation of encephalitis in a man with a pallidopyramidal syndrome of encephalitic origin.

History.—A man, aged 34, was admitted to the hospital in 1925, with an unimportant family history, except that his mother, aged 61, had a tremor of the lips, face and hands and was unstable emotionally. The patient was an only child and had been married twelve years. He had been in excellent health until the onset of the present illness. In April, 1920, he noticed severe pain in the right side of the back, radiating around behind the right ear and over the left eye to the middle of the forehead. This pain occurred in paroxysms at intervals of a few minutes, lasted only a few seconds, and was described as feeling like a hot iron wire in the flesh. It disappeared in two weeks and then appeared in both arms, where it was of the same nature, beginning at the neck and radiating down the front of the upper arms and along the radial borders of the forearm into all the finger tips. The pain lasted six months. On the appearance of the pain in the arms, the patient observed that he felt drowsy and dropped off to sleep readily in the daytime. The drowsiness lasted only one month and disappeared without further signs. In 1923, he noticed drooping of both eyelids, which gradually progressed and persisted up to the time of entrance into the hospital. He denied diplopia at any time. Simultaneously with the appearance of the drooping of the lids was the occurrence of stammering, salivation and increasing rigidity. In addition, he became troubled at this time with a spasm of the eyelids. They would suddenly go into a spasm, closing completely and remaining so for several minutes unless he pried them open with his fingers. He thought the left eye was worse than the right. These contractions were painful and increased in severity, together with general stiffness. For this reason he entered the hospital.

Examination.—The patient was well preserved. General examination gave practically negative results. He had a great deal of saliva in the mouth

* From the Philadelphia Orthopaedic Hospital and Infirmary for Nervous Diseases, service of Dr. T. H. Weisenburg.

with stomatitis as a result, and there were several carious teeth. The tonsils were not diseased. The thyroid was normal in size. The heart and lungs were normal. The blood pressure was: systolic, 130; diastolic, 80. The abdomen showed no gross abnormalities.

Neurologically, the patient showed a smooth, apathetic, waxlike facies, with an anxious look at times. He drooled saliva constantly and spoke indistinctly with what he described as a stammer, but which was in reality a spastic speech. The head was held flexed slightly forward. The upper and lower extremities were rigid, the former being held semiflexed with the fingers of both hands strongly flexed and clenched. There were fine and coarse tremors of the fingers and arms while at rest. A definite cogwheel sign was readily demonstrable in

Fig. 1.—Patient at rest, without palpebral spasm. The parkinsonian attitude is apparent.

either arm or leg. The muscles of all four extremities were stiff to passive movements. All active movements were slow and sluggish and were accompanied by coarse tremor. The gait was stiff and slow, with the body bent forward and the legs held stiffly. Examination of the cranial nerves showed the left palpebral fissure smaller than the right. The pupils were unequal and irregular and reacted sluggishly to light. There were no extra-ocular paralyses. The left side of the face, especially the angle of the mouth, seemed flatter than the right, which was drawn up at the mouth, but no weakness could be demonstrated objectively. The tongue was protruded in the midline with a coarse tremor. The other cranial nerves were normal. The reflexes were everywhere hyperactive and equal. The abdominal reflexes were absent, and there was a bilateral Babinski sign without ankle or patellar clonus.

Laboratory Examination.—The urine showed a specific gravity of 1.025 without any albumin, sugar or casts. The red blood cells numbered 4,860,000;

the hemoglobin was 85 per cent; white cells, 9,000. The blood chemistry showed: sugar, 98 mg.; nonprotein nitrogen, 32 mg. per hundred cubic centimeters. The blood Wassermann reaction was negative with all antigens. The spinal fluid showed: cells, 4; globulin, normal; the Wassermann reaction was negative with all antigens, and the colloidal gold reaction was 0000000000.

Description of Attacks.—The patient had many attacks of spasm of the eyelids. Without warning the lids would suddenly close and go into a state of extreme contraction, so that both eyes were screwed up tightly (fig. 2). The right eye always seemed more affected than the left. At the same time, the face was drawn up on both sides. At first, this was thought to be caused by the fact that the patient was in pain, but he denied having pain during the spasms and

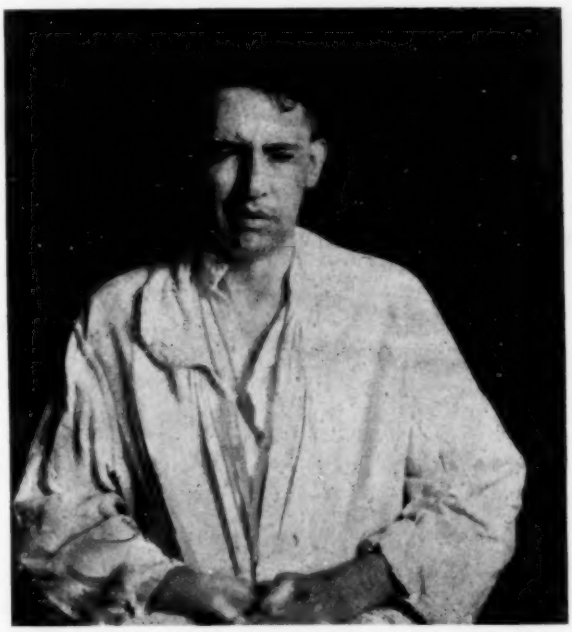

Fig. 2.—Patient shortly after the onset of an attack of palpebral spasm.

said that his face was screwed up when his eyelids closely so tightly. This involvement of the face was never marked but was nevertheless noticeable. If the eyelids were left alone during one of these spasms, they remained contracted for from one and one-half to two minutes by actual timing, and then relaxed sufficiently for the patient to open his eyes. Usually, however, the discomfort of the attacks was so great that the patient pried open the left eyelid by pushing upward just under the left eyebrow (fig. 3). After a few seconds the left eyelid would open, and with it the right eyelid. He said he always pried open the left eyelid because it did not contract as firmly as the right. Such attacks occurred frequently while he was in the hospital. They came on suddenly, at irregular intervals, usually at the rate of from fifteen to twenty-five a day. No vasomotor phenomena were observed during the attacks. Emotion seemed to have no effect in producing them. In every instance they came on involuntarily.

COMMENT

Spasm of the eyelids following encephalitis is not common. It has been described briefly by a few French authors, but no observations on this phenomenon have been found elsewhere. Apert and Vallery-Radot,[1] in 1921, demonstrated a case before the Pediatric Society of Paris. This case was in a child, aged 14, who, a year following an acute attack of encephalitis, developed a hemispasm of the right side of the face, with an attendant palpebral spasm on the same side. There were no other manifestations of encephalitis, and no effort was made to localize the lesion. Guillain, in 1922, is reported by Papastratigakis[2] to have related before the Paris Neurological Society the occurrence of spasmodic contracture of the eyelids produced by voluntary closing of the eyes. The latter

Fig. 3.—The method employed by the patient to pry open the eyelids.

reports a case of a man, aged 24, who in 1920 developed an acute attack of encephalitis lasting twenty-five days. Following the acute attack, a typical parkinsonian state developed; this gradually disappeared and was followed by spasm and inability to open the eyelids. There were no spasms elsewhere, but accompanying the palpebral attacks was a quasicontraction of the frontal muscles. Lemos[3] reports a case of postencephalitic parkinsonism with palpebral spasm

1. Apert, E., and Vallery-Radot, P.: Rechute d'encéphalite lethargique sous forme de spasme facio-palpébral, Bull. Soc. de pédiat. de Paris **19**:22, 1921.

2. Papastratigakis, M.: Spasme palpébral chez un parkinsonien post-encéphalitique, Rev. neurol. **39**:1019, 1922.

3. Lemos, M.: Intermittent Claudication, Cramps in Writing, Spasm of Muscles of Mastication, Glosso-Palato-Laryngeal and of the Upper Extremities, Appearing in Course of Post-Encephalitic Parkinsonian Syndrome. Probable Striate Localization, Rev. neurol. **2**:425 (Nov.) 1924.

but with spasm also in many other groups of muscles. Paulian[4] recently reported four cases of palpebral spasm after encephalitis. These represent the largest and most carefully reported group of cases. The first case was in a man, aged 20, who two weeks after an acute attack of encephalitis developed rapid respiration, trouble in vision and trembling of the fingers of the right hand. He showed an involuntary spasm of the eyelids with firm closure of the eyes, which lasted about one minute and was attended with rhythmic movements of the lids at the rate of about eighty a minute. The second case was in a patient having a post-encephalitic parkinsonism who at times developed a spasm of the upper eyelid during which the lid was drawn upward together with the eyeball. At other times the eyelids were tightly closed in violent spasm and could not be opened until the spasm had disappeared. The third case was similar. The fourth case presented typical tonic spasms of the eyelids. When told to close his eyes it took the patient some time to do so, but as soon as he did close them the eyelids went into tonic spasm lasting a minute or slightly longer. Cadwalader,[5] in 1914, reported a case almost identical with ours. His patient had spasm of the eyelids, and was unable to open the eyes without assistance. "At times when both eyes would be closed naturally, the eyelids would remain closed and could not be opened voluntarily; when, however, the patient placed his index finger on one orbital ridge and pushed upward, both lids could be elevated and the eyes remained open." Cadwalader ascribed this condition to lenticular degeneration.

From these cases, and from one of our own, it is possible to make a few observations on the nature of the palpebral spasms occurring after encephalitis. In the first place, it is comparatively rare if one judges by the number of instances reported. In every case it has been a late sequela of encephalitis, occurring at varying intervals after the acute attack. In our case, it occurred three years after the acute illness, simultaneously with the development of a parkinsonian state. Others have reported it from seven months to four years after the onset of the encephalitis. The spasm is always involuntary, but in one case of Paulian's it could be brought on by voluntarily closing the eyelids. Nothing seems to relieve the attack. Our patient could terminate it by prying open his eyelids, but usually the only remedy has been to wait until the spasm terminated. The number of the spasms varies in the different cases reported. It is difficult to give exact figures, but it is safe to say that in every case they occurred many times during the day. The duration is usually of one or two minutes, rarely longer. The spasms are tonic in character, but in one case of Paulian's, minor clonic twitchings were observed at the same time. In practically all instances it has been observed as part of a parkinsonian state, but it may occur as the only manifestation of a postencephalitic condition, as shown by the cases of Apert and Vallery-Radot. The spasm involved both eyes and in a few cases implicated also the muscles of the face. In none of the cases reported was only one eyelid involved. It is beyond the power of the patient suffering these attacks to do anything to prevent them. They appear absolutely involuntarily, but in some instances are preventable in that they do not appear until the eyes are closed.

Great difficulty arises when one attempts to localize the lesion responsible for these attacks. No autopsy material is available. Similar spasms have been observed, however, in the eyeballs in cases of postencephalitic parkinsonism during

4. Paulian, D.: Paradoxic Ocular Disturbances in the Course of Sequelae of Encephalitis Lethargica and of Parkinsonism, Paris méd. **2**:409 (Nov. 14) 1925.

5. Cadwalader, W. B.: Progressive Lenticular Degeneration, J. A. M. A. **63**:1380 (Oct.) 1914.

which the eyes are moved forcibly either upward or laterally. These attacks also are tonic in character, and are similar in many respects to those seen in the eyelids, except that they often last much longer. These spasms also occur involuntarily, last from several minutes to hours, occur frequently in parkinsonian conditions, and are sometimes associated with spasms of other groups of muscles, such as the muscles of the neck, the muscles of mastication and even those of swallowing. Such cases have been reported by Duverger and Barré,[6] Demetre and Grigoresco,[7] Fischer,[8] Springlova,[9] Ewald,[10] Marinesco, Radovici and Draganesco,[11] Hohman,[12] Popowa,[13] and Kulkow.[14] In none of these cases, however, has there been autopsy material available to determine the localization of the lesion causing the violent spasms of the eyeballs. Many theories have been offered. Duverger and Barré consider that the spasms are due to hypertonia of a reflex nature, labyrinthine in origin. Ewald and Fischer ascribed them to irritation of the corpora quadrigemina, and Kulkow favored a striatal localization. In the absence of necropsy material, any attempt at localization is uncertain. However, the tonic nature of the spasms would favor a striate localization if one considers the striatum as a tone-regulating mechanism. Jakob[15] believes that both striatum and pallidum influence muscle tone. In addition, the occurrence of these attacks, chiefly, if not almost entirely, in parkinsonian conditions, can hardly be looked on as incidental. These two facts point strongly to a localization of the lesion in the corpus striatum, though of course it is impossible to say dogmatically that this is so. The basal ganglia, however, have been too often blamed for clinical pictures that are puzzling and uncertain. The pathologic condition in this case is explainable on a more rational basis. The patient had a syndrome that involved not only the extrapyramidal but also the pyramidal system. He had a bilateral Babinski sign. Lhermitte and McAlpine[16] have

6. Duverger, C., and Barré, J. A.: Troubles of Associated Movements of the Eyes in Tabes, Parkinsonism, Epidemic Encephalitis and in Labyrinthine Disorder, Rev. neurol. **37**:439 (May) 1921.

7. Demetre, P., and Grigoresco, D.: Sur un état de parkinsonisme rappelant un syndrome analogue du spasme de torsion, Rev. neurol. **39**:1403, 1922.

8. Fischer, B.: Ueber vestibulare Beeinflussung der Augenmuskelstarre bei der Encephalitis epidemica, Deutsche Ztschr. f. Nervenh. **81**:164, 1924.

9. Springlova, M.: Eye Movements in Chronic Encephalitis, Čas. lék. česk. **63**:916 (June 14) 1924.

10. Ewald, M.: Conjugate Deviation of Eyes and Head After Epidemic Encephalitis, Monatschr. f. Psychiat. u. Neurol. **57**:222, 1924.

11. Marinesco, G.; Radovici, A., and Draganesco, S.: Hypertonic Paroxysmal Attacks of Conjugate Deviation of Head and Eyes in Post-Encephalitic Parkinsonism, Rev. neurol. **1**:148 (Feb.) 1925.

12. Hohman, Leslie B.: Forced Conjugate Upward Movements of the Eyes, J. A. M. A. **84**:1489 (May 16) 1925.

13. Popowa, Nina: Tonic Spasms of the Eye Muscles in Epidemic Encephalitis, Ztschr. f. d. ges. Neurol. u. Psychiat. **97**:515 (July) 1925.

14. Kulkow, A. E.: Periodic Ocular Spasm in Post-Encephalitic Parkinsonism, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:636 (June) 1926.

15. Jakob, A.: Die extrapyramidalen Erkrankungen, Berlin, Julius Springer, 1923.

16. Lhermitte, J., and McAlpine, D.: A Clinical and Pathologic Resumé of Combined Disease of the Pyramidal and Extrapyramidal Systems, with Especial Reference to a New Syndrome, Brain **49**:157 (June) 1926.

described a pallidopyramidal syndrome following encephalitis. In one case, which came to necropsy, the lesions were in the pallidum and the pyramidal tracts. It is probable that our patient has a similar lesion. If this is so, it seems reasonable to assume that an irritation of the facial centers in the cortex or in their corticifugal course could produce a faciopalpebral spasm such as is illustrated in our case. Le Damany [17] has recently asserted that the crossing of the superior facial fibers, whereby the muscles of the upper part of the face receive bilateral innervation, occurs in the subthalamic region. If this is so, a lesion here could cause symptoms similar to those observed in our case, and would be the more probable because it would be localized in an area that is often involved in encephalitis.

CONCLUSIONS

1. Palpebral spasm is a rare manifestation of epidemic encephalitis.
2. It occurs as a late sequela, usually in a parkinsonian state.
3. It is characterized by involuntary, tonic spasms of the eyelids, lasting one or two minutes and producing violent closure of the eyes.
4. The lesion is probably located in the subthalamic region.

ENCEPHALITIS WITH TUMOR OF THE BRAIN

REPORT OF A CASE *

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The differential diagnosis of encephalitis, cerebral thrombosis and tumor of the brain sometimes offers considerable difficulty, which is increased when two of the conditions are coincident. In the case reported below all three were present. Another reason for reporting this case is the finding of an organism in the blood stream during life and in the brain after death — an organism that Evans and I have isolated from several cases of epidemic encephalitis. We believe that it was the cause of the "idiopathic" paralysis agitans in this patient.

REPORT OF CASE

Clinical History.—S. K. H., aged 56, a public school teacher, always high strung and a hard worker, had had an intermittent rhythmic tremor of the right hand since the summer of 1925. At various times also she had had neuritic pains in the arms, for which nine teeth had been extracted in October, 1925. This operation was followed by "spells," which consisted of disagreeable sensations in the roof of the mouth, and which appeared particularly during periods of nervous tension. These manifestations were considered to be functional. Her present illness began with an acute attack on June 5, 1926, after several days of entertaining. The initial symptom was a severe headache which lasted for forty-eight hours and terminated in a crisis of dizziness and nausea. That same evening she lay down about 5 o'clock and when her son,

17. Le Damany: Presse méd. **63**:1, 1917.

* From St. Elizabeth's Hospital.

a physician, tried to rouse her at 9 she was inert and could not be roused. When she regained consciousness a short time later, she was found to be grossly aphasic. Paralysis was not noted, except for a slight diminution in the expressional movements of the right side of the face. Convalescence was slow and stormy. At times during the next few weeks she was restless and almost violent. At other times she would sleep for eighteen hours at a stretch. The headache had disappeared; fever and diplopia were not noted.

On June 24, she again lapsed into coma for three days, and was then removed to a hospital. The blood count at that time showed leukocytosis of 13,500 and 14,000; the urine and blood chemistry observations were normal. The spinal fluid was under increased pressure and contained an increased number of cells. The Wassermann and colloidal gold reactions were negative. The eyegrounds were obscured by vitreous opacities, but retinitis was not present.

Neurologic examination showed considerable variation from day to day. One day there was paresis of the right side of the face, but it receded before evening; at another time a patellar reflex was not obtained on the right side; at still another time the right leg appeared anesthetic, but these signs were inconstant. The skull was tender to percussion above the left temporal region, and the patient held her head rather fixedly. During the last few days of June the coma became intermittent, and on July 4 she became restless again. She apparently recognized her children, but could not call them by name. She repeated certain words and phrases over and over again, but could not carry on a conversation.

Examination.—On admission to St. Elizabeth's Hospital, July 14, 1926, the patient smiled pleasantly and nodded her head knowingly, but she caught only the general trend of questions and was unable to finish a sentence. A stenogram reads: "Well, so to speak, I have fixed a semester upon us. I have been looking up on this place in here so to speak. A regular semester he said we got so to speak. I really don't know any — well, nothing more." Enunciation was clear, the words were well formed, but misapplied, the syntax was inaccurate and objects were either miscalled or not named at all. The patient showed perseveration, using long words like "semester" and "curriculum," which arose from her occupation as a teacher, but recognized the correct words when they were given to her. Orientation, insight, judgment and memory could not be tested on account of the aphasia present.

She had a tendency to fall backward and to the right. The right side of the face showed moderate limitation in emotional expression. The pupils were equal and responded to light and in accommodation. Ocular rotations appeared normal. The eyegrounds were still obscured. Muscular power was reduced in the right hand. There was intermittent parkinsonian tremor in the right hand, with increased muscular tonus and cogwheel resistance to passive extension. Tendon reflexes were increased. The right lower extremity did not show variation from the left, except that the patellar and achilles reflexes were slightly more prompt. The Babinski sign and clonus, tremor and rigidity were all lacking.

Course.—During her stay in the hospital her temperature was about 100 F., and she showed a slight leukocytosis. She seemed to be improving. On July 20, however, she suddenly lapsed into coma. Blood pressure was 88 systolic and 60 diastolic. Cardiac stimulation revived her to a considerable degree, but the language disturbance was more marked, amounting to almost complete

aphasia. Paralysis was not present, nor was the Babinski phenomenon. Two days later, another attack of unconsciousness supervened, associated with rising fever. A blood culture made by Miss Evans was positive for a small gram-positive diplococcus of considerable virulence, which was identical with that isolated from other cases of encephalitis by Evans and myself.[1] Serum injection and blood transfusion failed to lower the temperature or to bring back consciousness. Instead, the temperature followed the "forty-five degree" course of medullary compression and reached 108 F. at the time of her death, on July 31, 1926.

The diagnosis was chronic encephalitis, which caused the parkinsonian tremor of the right hand and which was lighted up to renewed activity by the occurrence of cerebral thrombosis. The acute onset of symptoms and the finding of the organism associated with encephalitis ruled out the diagnosis of cerebral tumor, although the progress of the aphasia and the terminal rise in temperature would otherwise have suggested it strongly.

Postmortem Examination.—Necropsy was performed one hour after death. It revealed a well developed, somewhat obese, middle-aged woman. The heart was somewhat dilated, the myocardium soft and turbid. The lungs were edematous. The gallbladder contained two stones; the pancreas was infiltrated by fat; the kidneys were normal, and the endocrine system was without apparent lesions.

When the dura was reflected, the convolutions on the left side were found to be flattened, the fissures obliterated and fluid practically absent. The left hemisphere weighed 80 Gm. more than the right, and bulged obviously in the temporal region. The mammillary bodies and the chiasm were displaced to the right. The ventricles contained only a little fluid, and the left thalamus extended over the midline. Palpation of the temporal lobe revealed an irregular mass, which on section was found to be an invading growth, measuring about 3 by 5 cm., fairly firm, with indefinite boundaries, yellow but not hemorrhagic. It arose apparently in the first temporal convolution and in the insula. It extended into the second temporal convolution nearly to the temporal pole, and involved the external capsule and part of the parietal lobe. It did not extend into the precentral or hippocampal regions. A small projection or secondary growth was situated in the putamen, but the globus pallidus and internal capsule were not invaded. Near the center of the main growth was a rough-walled cyst which contained about 5 cc. of yellowish fluid, probably the result of thrombotic softening. The brain was soft and bulging as a whole. The uncinate gyrus on the left side was lacerated by pressure on the incisura tentorii, and the cerebellum and medulla showed compression cones about the foramen magnum.

Section through the mesencephalon revealed a thin locus niger on both sides, and the central portion on the left side was paler than normal. Microscopic examination revealed moderate atrophy on both sides of the nigral tissue, particularly in the dorsomesial portion on the left. The perivascular spaces were widely dilated (fig. 1). Small amounts of fat around the blood vessels in this region showed that the process of disintegration was active, and a few lymphocytes about a vessel or two suggested an inflammatory origin. Moreover, the same organism that was isolated from the blood was also cultivated from the mesencephalon.

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1. Evans and Freeman: Studies on the Etiology of Epidemic Encephalitis. I. The Streptococcus, Pub. Health Bull. **41**:1097 (June 4) 1926.

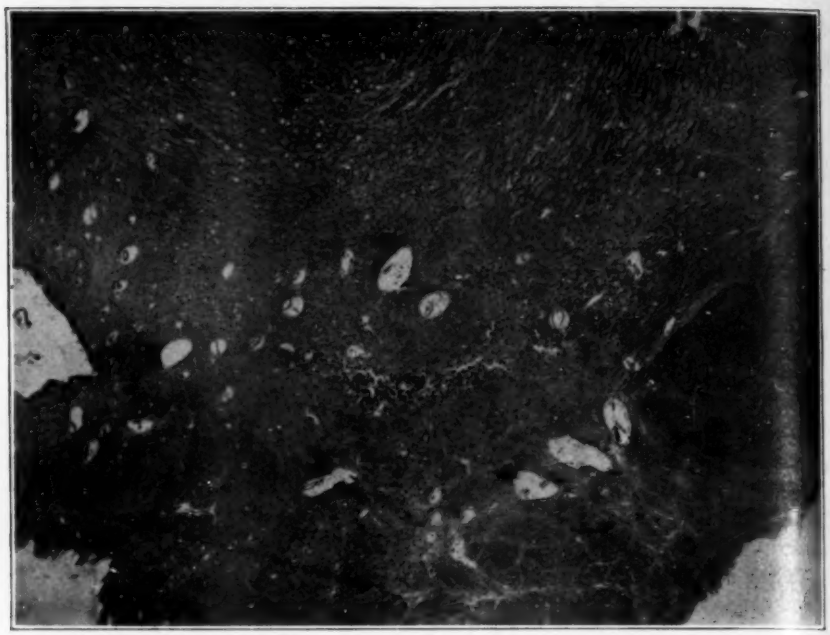

Fig. 1.—Locus niger of the left side from above. Disappearance of pigmented cells from the dorsal and mesial areas; wide perivascular spaces.

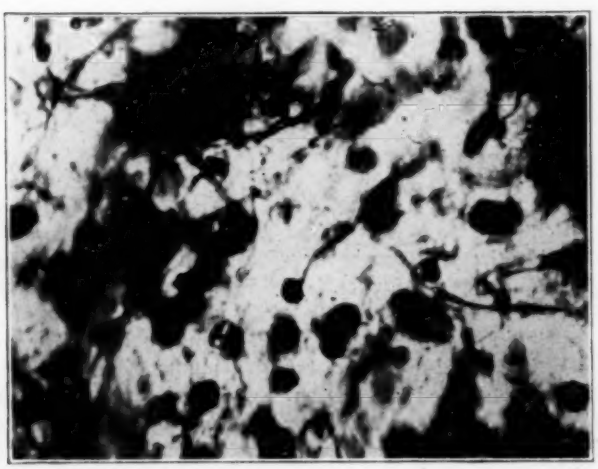

Fig. 2.—Spongioblastoma multiforme of the left temporal lobe, Hortega impregnation, unipolar cell in center, multipolar cell at the upper left portion.

The tumor was of the cellular type, with large areas of necrosis. The arrangement about the blood vessels was striking. The cells varied greatly in size and shape. Some were unipolar, others were multipolar, and they responded better to Hortega impregnations than to the Cajal stain (fig. 2).

The final diagnosis was acute epidemic encephalitis on a chronic parkinsonian basis, associated with a multiform spongioblastoma of the left temporal lobe, with thrombosis and cyst formation.

The patient's daughter-in-law, who nursed Mrs. H. through the first part of her illness, has recently developed acute encephalitis.

HERPES ZOSTER WITH PARALYSIS OF ABDOMINAL MUSCLES AND POSTHERPETIC NEURALGIA*

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The following report of a case of herpes zoster of the right twelfth thoracic nerve is of interest because of the rarity of paralysis following herpes of the trunk.

REPORT OF A CASE

History.—D., aged 60, entered the Wisconsin General Hospital on April 11, 1926, complaining of pain in the right side of the abdomen. He gave a history of having had "shingles" in February. Three weeks after the onset and just after the condition healed, he began to have pain below the ribs on the right side. The pain was described as a "numb feeling" when the patient was resting quietly, but intense on movement. The remainder of the history failed to give additional facts related to his chief complaint, with the exception of constipation since the onset of herpes, and the loss of 20 pounds (9 Kg.) in weight since February.

Physical Examination.—Examination revealed an obese man who turned gingerly in bed, sparing his right side. When he walked he supported the right side of the abdomen with his hand. Inspection showed the presence of catarrhal otitis media on the left side, rhinitis and oral sepsis. Movement of the base of the right side of the chest was limited. There was a marked hyperesthesia in the right side of the upper half of the abdomen following the lower border of the ribs from the axillary line to the rectus muscle, relieved somewhat by firm pressure. There was bulging in this region, even in the reclining position, and the muscles were found to be flaccid. Increasing the intra-abdominal pressure and standing increased the deformity. Healed pigmented scars extending anteriorly from the spine just above the iliac crest to the linea alba indicated that the twelfth posterior root segment was involved in the primary sensory disturbance.

Diagnosis.—The diagnosis was postherpetic neuralgia and paralysis of muscles supplied by the tenth and eleventh thoracic nerves following herpes zoster of the posterior division of the twelfth thoracic nerve.

While a great many cases of postherpetic complications have been reported, it will be noted that most of these have affected the cephalic extremity.

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Numerous examples of paralysis of the ocular muscles following herpes ophthalmicus, of facial paralysis following herpes of the face, neck, scalp and ear and of paralysis of the upper extremity complicating brachial herpes have been recorded. One case of paralysis of the vocal cord following thoracic herpes has been reported. But involvement of anterior roots is a rare complication, especially when one considers the relatively frequent occurrence of herpes zoster of the trunk.

It has been said that approximately 76 per cent (Hewlett, quoted by Netherton[1]) of cases of herpes involve the trunk, although the paralysis and other complications are more common in herpes of the cephalic extremity. It was of interest, therefore, to scan the literature with special reference to motor and postherpetic sensory disturbance following herpes of the trunk. Reports of thirty-three such cases were found, the majority having been reported by Ramsay Hunt[2] and Soderbergh.[3] The former reported 158 cases in 1909, with motor involvement of the trunk in eighteen; the latter, ten cases with motor involvement of varying degrees, with only one of complete paralysis. In the one, the protrusion was so marked that the patient entered the hospital for "abdominal pseudo-hernia." The complaints that led to the discovery of the paralyses are diverting and not included in most discussions of tumors of the abdomen. Two cases occurred in elderly men (aged 60 and 61) who consulted physicians because of abdominal tumor. Taylor[4] and Charron[5] each reported one case. The patient in Worster-Drought's[6] case complained of rupture, occurring twelve days after the onset of herpes of the twelfth thoracic nerve. In 1924, Bloedorn and Roberts[7] reported a case of paralysis of muscles innervated by the eleventh thoracic nerve occurring two days after the onset of herpes associated with hyperesthesia in the same segment. Juergens[8] reported a case similar to the one I have described, except that in my case the patient did not complain of pain. The patient in Juergens' case was a man, aged 66, who was seen two weeks after the onset with typical herpes along the course of the tenth thoracic nerve. Results of a physical examination were negative, except for pyorrhea and constipation, the latter having been aggravated by the herpes. A week later, or three weeks after the onset, he was seen because of "tumor" of the abdomen and constipation. Protrusion of the abdominal wall was increased by standing and by increasing the intra-abdominal pressure. There was, of course, not a real tumor, but a flaccid paralysis of muscles in that area.

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1. Netherton, E. W.: S. Clin. of N. Amer. **4**:1041 (Aug.) 1924.

2. Hunt, J. Ramsay: The Paralytic Complication of Herpes Zoster of Cephalic Extremity, J. A. M. A. **53**:1456 (Oct. 30) 1909.

3. Soderbergh, G.: Syndrome Moterus del' abdomen en presence de zona intercostal, Acta med. Scandinav. **54**:170, 1921.

4. Taylor, F.: Case of Shingles Followed by Paralysis of the Abdominal Muscles, Guy's Hosp. Rep. **52**:37, 1895.

5. Charron, Louis: Neurite zosterienne du tronc, J. de méd. de Bordeaux **92**:588, 1921.

6. Worster-Drought, Cecil: Herpes Zoster with Localized Muscular Paralysis, Brit. M. J. **1**:970, 1923.

7. Bloedorn, W. A., and Roberts, L. J.: Herpes Zoster with Motor Paralysis, J. A. M. A. **82**:622 (Feb. 23) 1924.

8. Juergens, H. M.: Herpes Zoster with Motor Paralysis, J. A. M. A. **82**:1342 (April 26) 1924.

Postherpetic neuralgia has not called forth a great deal of comment, although Osler[9] takes account of it and indicates its significance when he says that the harassed victim may commit suicide because of it. In my case, it was the chief complaint, being acute enough to prevent the patient from practicing his profession.

It is not within the scope of my experience to discuss in detail the pathology, although a statement of the prevailing theories might not be amiss. Most neuropathologists regard the essential lesion of herpes zoster to be an inflammation of the sheath of the ganglion with hemorrhages and round cell infiltration into the ganglion itself. This idea was first brought forth by Barensprung[10] in 1861 and later elaborated by Head and Campbell.[10] The inflammation, then, in these rare cases of motor complications extends from the posterior ganglion to the sheath of the motor nerve, which is in close anatomic relationship with the posterior ganglion, and which results in a motor neuritis. Montgomery[11] has fostered the theory that the primary infection is peripheral, traveling from a local lesion through an abrasion of the skin along the sheath of the nerve by means of perineural lymphatics. He bases the predomination of the occurrence of paralysis in the cephalic extremity on the anatomic relationship of the motor and sensory nerves to the skin. In the trunk the motor nerves are less accessible, whereas in the arm and head they are more superficial. The former seems a more logical and scientific explanation. The fact that the geniculate, otic, gasserian, and less often the sphenopalatine, ganglia as well as the ganglia of the posterior cervical chain are more frequently involved than those of the trunk favors this explanation, since they are in closer association by proximity and by communicating branches.

For those interested in postherpetic complications, attention is directed to an article by Weber[12] containing a bibliography of cases reported in the literature previous to 1916.

MYASTHENIA GRAVIS WITH OPHTHALMOPLEGIA AND CONSTITUTIONAL ANOMALIES IN SISTERS

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The two cases reported were studied in the service of Dr. T. H. Weisenburg at the Philadelphia Infirmary for Nervous Diseases. The chief interest rested in the fact that the patients were sisters, with symptoms and signs that seemed to justify the diagnosis of myasthenia gravis. The rarity of the occurrence in sisters is easily confirmed by a review of the literature of the condition.

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9. Osler: Principles and Practice of Medicine, ed. 10, New York, D. Appleton & Company, 1925, p. 1092.

10. Quoted by Worster-Drought: Herpes Zoster with Localized Paralysis, Brit. M. J. **1**:970, 1923.

11. Montgomery, D. A.: Herpes Zoster as a Primary Ascending Neuritis, Arch. Dermat. & Syph. **4**:815 (Dec.) 1921.

12. Weber, F. Parkes: Herpes Zoster: Its Occasional Association with a Generalized Eruption and Its Occasional Connection with Muscular Paralysis: Also an Analysis of the Literature of the Subject, Internat. Clin. **3**:185, 1916.

REPORT OF CASES

CASE 1.—The younger sister, Anna F., showed the more pronounced symptoms, and the onset was earlier in her case. She was 17 years of age at the time of admission, June 18, 1926, but looked considerably older—probably about 21. The chief complaint was a general tired feeling, with general weakness in the muscles all over the body and inability to keep the eyelids open.

In the family history of the two patients, there is one significant fact: the father is said to have died of diabetes. The only significant fact in the history of Anna was the early onset of menstruation at the age of 11½ years. This was apparently normal until about 1923, when the menstrual periods became more frequent, about every three weeks, and increased in duration to six days. She said that for two weeks before the period, she feels weak and for five days after the period feels much stronger.

The present condition and complaints began at the age of 9 years, when she noticed gradual increasing weakness. This had been so marked in the two years prior to admission that it had caused her to seek hospital care; during the year prior to admission, the weakness had become so pronounced that she could scarcely walk a block without excessive fatigue. At the same time, she complained of drooping and weakness of both eyelids, and suffered from pain in the eyes on endeavoring to read. She observed that the weakness was more marked in the afternoon than in the morning. In June, 1924, she was admitted to the Mt. Sinai Hospital, New York, where the diagnosis of myasthenia gravis with the syndrome of encephalitis was made. She was admitted to the Infirmary for Nervous Diseases on June 18, 1926.

Physical Examination.—The patient was of short stature with a tendency to obesity and pallor. The breasts and abdomen hung pendulously like those of a woman of middle age. The musculature was generally weak and flabby, but showed no atrophy. The thorax was long and shallow and breathing was shallow, but there were no râles or signs of pulmonary or other form of tuberculosis. The heart showed slight enlargement with a systolic murmur over the apex which was not transmitted. The cardiovascular function, as measured by the Trentsch rating scale, was zero, showing deficient strength of the cardiac muscle. There were two abscessed teeth, which were subsequently extracted without noteworthy alteration in symptoms.

The cranial nerves were normal except for bilateral ptosis which was marked, as well as weakness of the extrinsic muscles of the eyeball, which prevented complete lateral and upper deviation of the eyes. This action was readily fatigued. No paralysis was noted in the limbs, but the strength was uniformly and generally diminished, and there was marked exhaustibility. No incoordination, no loss of tonus and no involuntary movements or tremors were observed.

Laboratory and other tests showed a trace of albumin but no glucose in the urine. The red blood cells numbered 4,610,000; the white blood cells, 10,600; the hemoglobin was 70 per cent. The fasting blood sugar varied from 87 to 111 mg. per hundred cubic centimeters; the nonprotein nitrogen and urea were within normal limits. The basal metabolic rate was plus 6. The blood and cerebrospinal fluid Wassermann reactions were negative. A roentgenogram of the thymus gland showed no enlargement. The sella turcica was normal in size and outline. The vertebral column showed a right dorsal, left lumbar scoliosis with slight rotation of the bodies. Sugar tolerance was subnormal, the blood sugar rising to 189 mg. per hundred cubic centimeters and remaining as high as 240 mg. at the end of the third hour, while the urine showed 0.09 per cent sugar.

At weekly intervals, the muscles were tested with faradic and galvanic currents, but no myasthenic reaction was evident, though the muscles of the lower extremities on occasion were found to react less promptly to faradism than to galvanism. Pharmacodynamic tests with epinephrine and pilocarpine showed greater reactivity to the former. A psychometric examination showed the intelligence to be that of a high grade moron.

CASE 2.—Sarah, the sister, was said to be 19 years of age but looked more like 25; she was the next older sister in the family and presented features less marked than, but similar to, those of the patient just described. The past history showed no more serious condition than measles at the age of 1 year. In 1924, tonsillectomy was performed, and adenoidectomy in 1925. The menses began at 14 years, much later than in the sister Anna. They were regular, lasting from four to five days, and no variations in symptoms were observed except for slightly increased weakness during the first two days of menstruation.

The present condition began at the age of 14, at about the onset of menstruation. She complained at this time of a sensation of heaviness and general exhaustibility, increased by a moderate amount of exertion. This condition has been specially pronounced during the last two years. She has felt stronger in the morning and more fatigued in the afternoon. At the age of 14, weakness and drooping of both eyelids was noticed, and in 1925, she underwent an operation for the relief of the ptosis, which enabled her to see better. Since June 30, 1926, she has complained of occasional diplopia, and at night the eyes feel extremely tired. Reading for an hour is sufficient to produce fatigue. She has shown no weakness or fatigability in mastication or deglutition, and no fatigue in talking. At the time of admission, Aug. 30, 1926, she was able to walk twenty-five blocks, she said, without fatigue. As in the case of her sister, there has been no decline in weight.

Physical Examination.—The patient was less obese than her sister and showed less tendency to pendulosity of the breasts and the abdomen and no visceroptosis. The lungs and heart were normal to ordinary means of examination. The ears showed evidence of residual otitis media. The cranial nerves and ocular muscles showed the same restriction of ocular movements in all directions. No paralysis or strabismus was observed; yet she complained of diplopia in all parts of the field of vision. This was shown to be associated with restriction of lateral and upward movements of the eyeballs. The facial musculature showed slight bilateral weakness with equal flattening of the nasolabial folds. The general muscular exhaustibility and weakness of the extrinsic eye muscles were the chief somatic complaints. She showed, however, a fairly good grip of from 60 to 70 Kg. in both hands, and when the action was repeated several times, she showed a rapid exhaustion. There was no dysmetria or dyssynergia. The reflexes were all hyperactive, and the plantar response on both sides was flexion. The pupils were normal and showed no fatigability.

Laboratory Examination.—There was a faint trace of albuminuria without casts. The red blood cells numbered 4,670,000, the white cells, 5,200; hemoglobin was 83 per cent. The average fasting blood sugar was 102.5 mg. per hundred cubic centimeters, and the nonprotein nitrogen and urea were normal. The basal metabolic rate was plus 6. The Wassermann reaction with the blood was negative. The sugar tolerance, as contrasted with that of her sister, was normal The roentgen ray showed no evidence of persistent thymus. The sella turcica was small but normal. For three weeks, the muscular reactions were tested, and no myasthenic reaction was found. When placed on a creatine-free diet, she showed only 7.88 mg. of creatine per hundred cubic centimeters in the

blood and a faint trace in the urine. Psychometric examination of this patient showed a similar level of intelligence to that of the sister; namely, that of a high grade moron with a mental age of 10 years plus.

COMMENT

The occurrence of metabolic disorders and of constitutional anomalies in cases of myasthenia gravis has been frequently demonstrated in recent years and these cases are presented as illustrations of the presence of some constitutional factor in the condition known as myasthenia. The occurrence of the same condition in two sisters is extremely rare and brings added support to the theory of constitutional deficiency as the ultimate causal factor.

A history of diabetes in the father of the patients and the presence of a much lowered glucose tolerance in the sister in whom the myasthenic symptoms were most pronounced should also be noted. Cases of myasthenia gravis have been reported by Brissaud and Lautzenberg with diabetes as a concurrent phenomenon, and Kojeinikoff has reported glycosuria, but in none of these cases, apparently, was the diabetes considered an important factor. In a case studied by Froboese Thiele and Leschcziner,[1] evidence of an early diabetes was also found with acetone and diacetic acid in the urine.

Oppenheim[2] has emphasized, by numerous examples, the importance of congenital constitution in myasthenia gravis, and many congenital anomalies have been shown. Thus, Curschmann[3] reported two cases with gonadal hypoplasia in females, and the occurrence of myasthenia with pregnancy has been noted. Perhaps the most important congenital endocrine anomaly has been thymus hyperplasia, and the frequency of new growths of a thymus gland in myasthenia gravis is well known through the work of Buzzard[4] and others. In a case reported by Claude and Porak,[5] an enlargement of the posterior lobe of the pituitary gland was also noted. These authors think it possible that the hypertrophy of these endocrine glands might be the result of a battle against some toxin.

In the cases described, there is evidence in the onset of the myasthenia in both girls at about the time of menstruation of a definite endocrine disturbance. At this time, one of the first symptoms was the weakness of the orbiculares oculi, and this was found in both cases. Oppenheim and Karplus have drawn attention to the frequency of ophthalmoplegic symptoms in myasthenia gravis, and they occur as the initial and, at times, the chief symptom of the malady. Particularly has this been demonstrated by Bielschowsky[6] in the case of a girl, aged 17, in which the main involvement was weakness and convergence of lateral movements of the eyes. In this case, as in the one reported here, the weakness of the lower extremities came later than the signs of ophthalmoplegia. According to Bielschowsky, paralysis of the external muscles of the eyes occurs in one third of all cases, and is the first symptom. The most regular and constant symptom of myasthenia gravis is the ptosis, which is present in 80 per cent of the cases; it is usually bilateral. Goldflam would diagnose myasthenia gravis by this exhaustibility of the lids alone, and Karplus has shown frequent paralysis of the associated movements of the eyeballs.

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2. Oppenheim: Lehrb. der Nervenkrankh. **2**:1635, 1923.
3. Curschmann: München. med. Wchnschr. **71**:1135, 1924.
4. Buzzard: Trans. Path. Soc. London **55**:357, 1905.
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Abstracts from Current Literature

STUTTERING. THE CAUSE AND CURE. JOHN A. GLASSBURG, M.D., Arch. Otolaryng. **5**:122 (Feb.) 1927.

Stammering is incorrect speech or mispronunciation, and stuttering is difficult speech. There is difficulty in pronouncing certain words with a resultant repetition, or there may be inability to speak at all or to respond when spoken to suddenly. The stutterer can speak correctly when he speaks at all, as evidenced by his ability to sing and talk to himself.

Etiology.—Makuen believed that heredity is a most important factor and found it in successive generations. Imitation from contact must be distinguished from what is due to a neuropathic taint. Cluttering is mental haste. It may be combined with stuttering, which is due to fear. The clutterer speaks more clearly the more he concentrates on speech, whereas the stutterer becomes more indistinct because he is already overanxious and conscious of his handicap. The author believes that stuttering is a spastic coordination neurosis caused by a mental conflict. Whatever other contributory causes there may be in the etiology of stuttering, the most important are a predisposing cause in the form of a neuropathic constitution and an exciting cause in the form of a nervous shock or psychic insult. The underlying predisposition is to be attributed to heredity. The shock may come from a fall, an operation, nervous exhaustion following exanthematous disease or severe acute infections, or from fear, embarrassment, anxiety, a frightful experience or the psychoneuroses. A girl began to stutter after her life had been threatened with a stiletto. A boy began to stutter when suddenly and abruptly called on to recite in the classroom. Another little boy found himself speechless after being told a gruesome ghost story by his brother while they were alone in bed at night; on regaining speech, he stuttered.

Diagnosis.—The diagnosis is self evident. Test phrases may be employed to determine the extent and severity of the disorder. The stutterer does not always stutter on the same sounds, and the character of the defect depends on the emotional state of the stutterer during the examination. Test phrases may be used to make a diagnosis. The patient must be willing to undergo treatment for at least a year and must cooperate.

Surgical Treatment.—Although, primarily, stuttering is a mental affliction, there are physical factors that may be associated and act as aggravators. These are adenoids, abnormal length and thickness of the uvula, abnormal size and tumors of the tongue, hemiatrophy of the tongue, cleft palate, harelip, deformities of the jaw, improper development of the palatal arch, imperfect dental arches, nasal polypi, hypertrophied turbinates, marked deviation of the septum, tongue tie and defective hearing.

Psychotherapeutic Treatment.—Stuttering has been defined as a spastic coordination neurosis based on a mental conflict. To determine the nature of this mental conflict, which has long since been forgotten and lies buried in the subconscious mind, hypnosis or psychanalysis may be employed. The nature of the conflict is discovered and revealed to the stutterer. The stored up and suppressed emotions are liberated, and through analysis and discussion a readjustment is established. Suggestion is also useful in creating a spirit of self-confidence, something the stutterer usually lacks. By positive sug-

gestion the stutterer is convinced that he can speak, that he is cured and that he is well. The patient may be distracted by various means, such as the metronome, the megaphone, singing or chanting, elongation of the vowels, pacing, writing, change of voice and breath-grouping.

The Metronome: The stutterer utters one syllable to the beat, thus distracting his attention; the rate is then increased.

The Megaphone: The patient repeats a sentence through a megaphone raising his voice as if about to shout. He is distracted, talks well and is then reassured and told that "it is only a lack of will and confidence that prevents him from talking well."

Singing and Chanting: This demonstrates to the patient that a sentence on which he has stuttered can be clearly and correctly enunciated and that there is no physical articulatory disturbance.

Elongation of Vowels: Have the patient say all words with the vowel elongated, gradually reducing the period of elongation.

Pacing and Writing: Pace the room pronouncing one word at each stride, causing distraction. Have him make a straight line for each syllable he pronounces. Being distracted, he speaks well while writing.

Change of Voice: Whisper one word, raise the voice on the next, lower it on the third, and shout on the fourth. The change of volume keeps his attention fixed.

Breath-Grouping: The patient is given a paragraph to read and is instructed to take the first word on the first breath, the next two words on the second breath, the next three words on the third breath, the next four words on the fourth breath and perhaps a whole sentence on the following breath.

Reeducation: Reeducation treatment by a specially trained teacher under the supervision of a medical speech specialist is classified under the following headings:

(1) Relaxation. When the stutterer begins to speak, he directs his attention to the process and becomes tense. The muscles contract, he stands rigid, the abdominal wall hardens like a board, the jaw is held tight, the lips are firmly compressed, the fists are clenched, the cheek muscles are taut and there is a spasm of the laryngeal muscles. Against this barrier of spasticity he throws a flow of speech which comes in a torrent of explosive utterances. The failure aggravates the situation, and he may become speechless. The first task is to break down the wall of spasticity and liberate the imprisoned voice. The muscles of the face, mouth, neck, larynx, abdomen, and in short, of the whole body, for one speaks with the entire body, should be relaxed. This cannot be done in classes with the children severely disciplined. The first requisite is a sympathetic relationship to gain the confidence of the patient who must be willing. He is made to feel thoroughly at home. His attention is distracted. Relaxation of the body as a whole may be obtained by the exercises which are described in detail in the article. Sets are given for the general musculature, for relaxation of posture, for relaxation of head and neck, for relaxation of arms, for relaxation of the hands, and the following for relaxation of the tongue: (a) Let the tongue hang loosely and relaxed from the mouth for a count of five. Ready, 1-2-3-4-5. (b) Repeat, saying, la-la; la-la; la-la; la-la. Ready, la-la; la-la; la-la; la-la; la-la. (c) Repeat, saying, la-la-la; la-la-la. Ready, la-la-la; la-la-la; la-la-la; la-la-la; la-la-la. (Note: the la, la, la should be said sleepily, each group more softly than the preceding one until the last is scarcely audible). (d) Repeat la-la-lively; la-la-lively, the voice being raised on "lively." Ready, la-la-lively; la-la-lively; la-la-lively; la-la-lively; la-la-lively.

The following exercises may be used for relaxation of the larynx and vocal cords: (a) Open mouth, inhale air and exhale easily five times. Ready, 1-2, 1-2, 1-2, 1-2, 1-2. (b) Sleepily, dropping head forward, say a. Ready, a-a-a-a-a. (c) Sleepily, dropping head forward, say e. Ready, e-e-e-e-e. (d) Sleepily, dropping head forward, say i. Ready, i-i-i-i-i. (e) Sleepily, dropping head forward, say o. Ready, o-o-o-o-o. (f) Sleepily, dropping head forward, say u. Ready, u-u-u-u-u. (g) Softly sing up the scale a. Ready, a-a-a-a-a-a-a. (h) Softly sing up the scale e. Ready, e-e-e-e-e-e-e. (i) Softly sing up the scale i. Ready, i-i-i-i-i-i-i. (k) Softly sing up the scale o. Ready, o-o-o-o-o-o-o. (l) Softly sing up the scale u. Ready, u-u-u-u-u-u-u.

(2) Breathing. Stutterers may or may not breathe properly, and defective breathing engenders stuttering, but the fact remains that stuttering nearly always causes wrong habits of breathing during speech. Exercises are given to correct breathing.

(3) Vocal Gymnastics. Though stuttering is a neurosis and is not caused by improperly functioning articulators, it is often associated with a physiologic disorder of these organs. The lips are spastic, the tongue is rigid, the soft palate is stiff and the muscles of the mouth and throat are taut. Consequently, not infrequently a secondary improper articulation is developed on top of the inability to speak. The following exercises have been devised to overcome the disorders of the articulatory organs: A. For tongue gymnastics: (a) Push the tongue outward and downward toward the chin out of the mouth. Ready, 1-2, 1-2, 1-2. (b) Push the tongue outward and upward toward the nose, out of the mouth, as far as possible, even touching the nose. Ready, 1-2, 1-2, 1-2. (c) Point the tip of the tongue upward and downward alternately. Ready, 1-2-3-4-5-6-7-8-9-10. (d) Rotate the tongue to the right, then down, then to the left, then up, then to position. Ready, 1-2-3-4-5; 1-2-3-4-5. (e) Protrude the tongue, grooving it at the same time by raising both sides. Ready, 1-2, 1-2, 1-2. (f) Curl the tip of the tongue back of the front teeth with the mouth kept open. Ready, 1-2, 1-2, 1-2. (g) Press the tip of the tongue back of the front lower teeth. Ready, 1-2, 1-2, 1-2. B. For lip gymnastics: (a) Protrude the lips in a puckered condition. Ready, 1-2, 1-2, 1-2. (b) Raise the upper lip, exposing the teeth. Ready, 1-2, 1-2, 1-2. (c) Wrinkle the nose so as to expose the upper teeth. Ready, 1-2, 1-2, 1-2. (d) Raise the right side of the upper lip. Ready, 1-2, 1-2, 1-2. (e) Raise the left side of the upper lip. Ready, 1-2, 1-2, 1-2. (f) Pull down the lower lip, exposing the lower teeth. Ready, 1-2, 1-2, 1-2. C. for the soft palate: (a) With the mouth wide open, say ah-ah-ah and watch the palate rise. Ready, ah-ah-ah-ah. (b) Yawn and watch the palate rise. Ready, yawn.

(4) Phonetics: Though there is no primary phonetic disorder in stuttering, bad speech habits are formed which require reeducation. Furthermore, the stutterer is more likely to stutter on certain sounds than on others. The most common of these are *p*, *b*, *m* and *w*. Phonetic exercises especially designed for the teaching of the proper pronunciation of these sounds are given; for the *p* sound under the captions, Production, Technic, Sound Drill, Word Drill, Sentence Drill and Rhyme Drill; also for *b*, *m*, and *w* sounds.

Summary.—Stuttering is a spastic coordination neurosis based on a mental conflict. The causes are a predisposing neuropathic constitution and an exciting factor in the form of a nervous shock or psychic insult. The treatment is threefold: surgical, psychotherapeutic and reeducational. The surgical treatment is directed toward the correction or removal of abnormal physical conditions in the vocal passages. Psychotherapy, in the form of a hypnosis, psycho-

analysis, autosuggestion, heterosuggestion and distraction, is directed toward unearthing the basic mental conflict and readjusting the personality. The reeducational treatment consists of a series of exercises under four different headings: relaxation, breathing, vocal gymnastics and phonetics. Stuttering is a curable condition, but it requires the combined efforts of the patient, the teacher and the physician to cure it.

HUNTER, Philadelphia.

THE PATHOGENESIS OF MULTIPLE SCLEROSIS. TADEUSZ FALKIEWICZ, Arb. a. d. Neurol. Inst. a. d. Wien. Univ. **28**:172 (May) 1926.

This contribution is devoted to a study of the formation of the patches in multiple sclerosis. At the present time there are two apparently contradictory theories in vogue. One, the vascular theory, in which it is assumed that the distribution of the patches follows the course of the vessels. Siemerling and Raecke, two prominent exponents of this theory, believe that the disease is due to some unknown exogenous factor which exerts its deleterious effect by way of the blood vessels as a result of which the areas surrounding them become affected so that the resulting lesions can hardly be distinguished from other myelitic lesions. In support of their theory these authors point to the occasional occurrence within the sclerotic foci of vessels whose walls show definite pathologic changes. Falkiewicz admits the truth of this, but he doubts whether one is justified in regarding the process as a vascular one in Siemerling and Raecke's sense. In the other theory propounded by Guillain, Bertrand and Marinesco, and others, it is assumed that the disease is due to an infection which reaches the cerebrospinal fluid by way of the lymph channels.

In contrast to the purely vascular theory, Marburg takes the view that multiple sclerosis represents a "discontinuation" process—a destruction of myelin analogous to that observed in periaxial neuritis. This does not necessarily deny that the process reaches the central nervous system by way of the blood vessels, but it is assumed that the process depends neither on disease of the vessels nor on perivascular alterations. Marburg's view is also significant because it tends to point to an exogenous genesis of the disease.

To determine the relationship of the sclerotic foci to the blood vessels, Falkiewicz studied carefully twelve cases of multiple sclerosis, in all of which the patients had been ill for a number of years. He examined serial blocks from 2 to 15 mm. in thickness in order to enable him to follow the lesions in toto. As a result of this study he is convinced that there occur in this disease a number of sclerotic foci that might wrongly be interpreted as vascular lesions. Some of these foci are typically wedge-shaped with the broad base at the periphery and the apex against the center of the cord; occasionally one sees a vessel in the center of the focus which appears as if it might have been the point of origin of a vascular disturbance. On examining, however, the section immediately succeeding this one in an orocaudal direction, an entirely different picture is observed; here the lesion has lost its typical wedge-shaped appearance and is irregular in outline. The "spotty" appearance of the myelinated fibers in the center of these foci is entirely different from that observed in compression syndromes. It is also noteworthy that some of these foci extend in a most irregular fashion toward the center of the cord, so that at the apex of the wedge there may be found a wider focus which involves only the gray substance of the external part of the cord. Another noteworthy feature is the fact that in the wedge-shaped foci in which vessels are found the latter are not always in the center of the focus; as a matter of fact they are more often found at the

periphery. When the foci are fully developed and completely sclerotic the vessels within the focus show no difference from those without it.

Within the lateral columns of the cord the lesions seem to have certain sites of predilection; they are generally found in the more dorsal parts nearer to the pyramidal tract; another favorite site is the anterolateral column. In the anterior column the region most frequently involved is that around the sulcus, where the lesions appear in the form of strips that are symmetrical on the two sides, or they may appear narrower ventrally and wider dorsally. The superficial location of some of the lesions is regarded by some observers as evidence that the process is derived from the meninges—perhaps in the nature of an infection of the subarachnoid space. Schmalz examined these cases carefully but could find no evidence of a primary meningeal involvement. The characteristic appearance of the patches in the posterior columns is striking; these are found in every case and always assume a typical position and typical shape resembling the oval lesions observed in closure of the vessels of the posterior columns; in some cases these foci also have a striking resemblance to the glial pegs found in syringomyelia. This appearance of the patches in this location would offer additional evidence against the "meningeal" theory.

The fact that in every case examined patches were found in the dorsal septum appears to the author to be of great genetic significance. It would seem that this region is an unusually vulnerable site for diseases of the cord, and that this unusual vulnerability may have some relationship to constitutional factors in the formation and closure of the central canal. The localization of the lesions in multiple sclerosis in the cord may also possibly be influenced by some such constitutional factors.

Altogether, it would seem that the similarity of the lesions in multiple sclerosis to genuine vascular lessions is only superficial; the mere form of the lesion does not justify the conclusion that there is a vascular process at the basis of the genesis of the disease. There is, however, one form of a lesion which must be mentioned in this connection. Borst and others have described small isolated foci surrounding a vessel in some rare cases of multiple sclerosis; these foci may remain isolated for ever; they may appear almost like the pale perivascular areas encountered in severe arteriosclerosis, or they may resemble the lesions observed in the cord in pernicious anemia. The proponents of the "vascular" theory point to this type of lesion as confirmatory of their hypothesis. Falkiewicz, however, believes that they occur too rarely and are altogether too small to give them pathogenetic significance.

As to the blood vessels themselves: In the old lesions with complete sclerosis the vascular degeneration is not uniform; as in every form of old sclerosis the vessel walls are thickened, the fibrosis involving only the media and adventitia. It is also noteworthy that one part of a vessel would show perivascular infiltration with granular cells, whereas another part of the same vessel would show a definite lymphoid infiltration of the adventitia with occasional plasma cells. The vascular changes are not limited to the vessels within the lesions; they may extend to the vessels in the meninges and to those in the sulcus longitudinalis ventralis. The changes in the meningeal vessels, however, are nothing like those observed in syphilis in which the adventitia is always affected and in which the lesion in the vessel itself is always much older than that in the parenchyma. The nearer the periphery is approached the more intense the vascular reaction, with its greatest intensity in the anterior spinal artery and in the meninges. This, in the author's opinion, would also seem to be against the theory that the inflammatory process in the vessels and meninges is the primary condition—it is more likely a secondary process, a complication.

Falkiewicz does not deny that the pathologic process producing multiple sclerosis has its origin in the blood vessels, but he believes that this occurs in a different manner from that claimed by the proponents of the "vascular" theory. In this disease one apparently deals with a virus which has a special affinity for myelin sheaths, not unlike the toxin which produces periaxial neuritis of the periphery; it is only later, much later, that the mesodermal elements begin to participate in the process; at the same time it is not impossible that this reaction depends on the breaking down of the parenchyma with its associated irritation. One must, therefore, conclude that the pathogenesis of multiple sclerosis depends on numerous factors which are complicated by inflammatory processes in the nature of a serous meningitis, and that there is no proof that the entire pathologic process is purely vascular in the nature of an inflammation.

KESCHNER, New York.

ENCEPHALITIS AND ITS EFFECT ON THE BEHAVIOR OF CHILDREN: 1. A STUDY OF POSTENCEPHALITIC BOYS IN A HOSPITAL SCHOOL. DR. DANIEL H. FULLER, ATLANTIC M. J. **30**:350, 1927.

Physicians connected with the Pennsylvania Hospital are undertaking a study of the rehabilitation of youthful sufferers from encephalitis. The patients were carefully selected with regard to age, and severe neurologic disorders were excluded. The program of training consisted of school, manual training, farming, gymnastics and particularly supervised recreation. Conduct was stressed before everything, and daily reports were turned in on each student. Repression and discipline were necessary at first but later became superfluous as the boys fitted into their environment. Penalties consisted in deprivations, being put to bed, meals alone or an hour or two in the bath tub. Corporal punishment, having failed at home, was never resorted to. Rewards for good behavior consisted in trips here and there and special privileges. "One of the most effectual punishments is the ignoring, for a half-day, of the culprit who has broken a rule or disgraced himself by some misconduct."

A court, composed of the group with one person as judge, arouses the boys' sense of fair play and makes its penalties more effective. The formation of new habits is a slow process, and the labor involved extremely great, but the results appear to be promising.

2. DIAGNOSIS OF POSTENCEPHALITIC CONDITIONS. DR. EDWARD A. STRECKER, Atlantic M. J. **30**:352, 1927.

Twenty-four boys and six girls, ranging in age from 18 months to 14 years were studied carefully during the months and years following the acute disease. Disturbances in behavior were of wide variety and usually of marked intensity. In only four of the group did serious behavior difficulties fail to develop. "Furthermore, the troublesome and dangerous behavior is not at all the result of deficient or defective intelligence. In only two of the cases in this series was there mental retardation. The change involves the personality of the child and practically reverses it, but spares the intellectual processes. It has been predicted that encephalitis may make a class of super-criminals." The acute symptoms were not a reliable guide, for they might be trivial and the behavior outrageous Usually, however, children over 16 or 17 did not succumb to these disorders. The development of paralysis agitans was usually associated with mild conduct disorders, but in those patients who showed other neurologic phenomena the behavior was but slightly better than in those who escaped neurologic damage.

3. General Considerations in Encephalitis as They Affect the Medical Profession. Earl D. Bond, Atlantic M. J. **30**:353, 1927.

The writer reports the results of the treatment of the group of patients mentioned in the first paper. After a lapse of two years the patients have shown definite improvement in behavior, and some children have been allowed to go home. The patients are much more easily treated in a group by those accustomed to behavior disturbances. "Superfluous energy has been drained off among themselves instead of extending outward to annoy people around them." "The good results from the group contrast sharply with poor results in the patients whom we have tried to treat individually." There was no evidence of any progressive physical disease in the two years that these patients were under observation. The feeling of inferiority, due partly to the physical defects left by encephalitis, may have aided in the development of bad behavior. A child showing these disturbances is rarely treated satisfactorily at home. Constant attention, even disposition and regular habits are essential in those who would take care of patients at home. The future of these patients is of interest because of the large number who are at present suffering from such behavior disturbances and who will later come to suffer from them. There is no institution prepared for them. It is interesting to speculate on the possibility of encephalitis being responsible for the habitual criminals and psychopathic persons. "Fewer criminals may be born bad and more may be made bad by disease and bad management afterward."

Freeman, Washington, D. C.

One Hundred and Sixteen Verified Intracranial Lesions with Report of Vestibular Tests. Their Value in Localization. Francis C. Grant and Lewis Fisher, J. f. Psychol. u. Neurol. **34**:113, 1926.

In the review of this series of cases, it is the accuracy of the vestibular reactions that is most impressive. Grouping together their results, these authors claim to have made correct localizations in 89.4 per cent of the cases. Certain groups of reactions seem to stand out as indicating lesions of definite areas. The cerebellopontile angle syndrome is clean-cut. Conjugate deviation of the eyes to the side of the lesion, a marked reaction to small doses of stimulation with normal cerebellar responses, or increase of nystagmus over vertigo, postulate a supratentorial neoplasm. Variations in the past-pointing and vertigo reactions are positive evidence of lesions in the cerebellar hemispheres. The largest number of errors were made in the group harboring tumors in this region. However, when it is remembered that any of the cerebral series of cases might have harbored a cerebellar tumor and that in only two of the verified supratentorial series was an error made in placing the lesion subtentorially when it was actually supratentorial, it seems that in the vestibular reactions one has a valuable means of differentiating between infratentorial and supratentorial pathology. Even when the matter is considered conservatively, negative evidence from vestibular reactions should be considered trustworthy even if a positive localization may be regarded as less valuable. The factor of intracranial pressure must always be taken into consideration in making a positive diagnosis of an infratentorial mass lesion. Supratentorial lesions may, if they give rise to increased intracranial pressure, yield responses simulating closely those of infratentorial lesions. Arachnitis about the cisterna magna, resulting in internal hydrocephalus and dilatation of the fourth ventricle, may reproduce a vestibular syndrome of a tumor in the vermis.

From a consideration of the vestibular responses from this series of cases, the authors formulate definite group responses as evidence of the location of mass lesions in a specific area of the brain:

1. Cerebellar lesions which give the following group reaction: (*a*) poor pelvic girdle movements; (*b*) marked tolerance to vestibular tests; (*c*) interference with vertigo and past-pointing responses; (*d*) predominant signs of increased intracranial pressure.

2. Lesions of the cerebellopontile angle: (*a*) totally impaired eighth nerve on the side of the lesion in both cochlear and vestibular divisions; (*b*) loss of function of the vertical canals on the opposite side, but normal function from horizontal canal with normal hearing.

3. Supratentorial lesions, midline or hemispheric: (*a*) marked susceptibility to vestibular stimulation; (*b*) conjugate deviation of the eyes to the side of the lesion; (*c*) exaggeration of nystagmic responses over the vertigo and past-pointing responses; (*d*) no evidence of cerebellar hemispheric lesion, although increased intracranial pressure may interfere with the responses from the vertical canal.

The authors' final conclusion is that in every case of suspected tumor of the brain, the evidence from the vestibular tests as to the location of the tumor should be carefully evaluated before a final decision as to the localization of the growth is reached.

The original article is in English, and contains abstracts of the clinical histories and postmortem and operative observations of the cases on which this contribution is based.

KESCHNER, New York.

THE THYMUS GLAND. W. WALTER WASSON, Arch. Otolaryng. **4**:495 (Dec.) 1926.

This is a study of 135 children under 2 years of age thirteen of whom were studied from birth to the age of 3. Serial roentgenograms with elaborate and careful technic were made immediately before and just after death in order to study the shadow of the thymus. By this method, the thymus gland in infants under 2 years of age can be accurately portrayed in a high percentage of cases. The great vessels form a triangular shadow which greatly narrows as it passes upward toward the first rib. At its narrowest point it is less than the transverse diameter of the shadow of the spinal column. "If the thymus is present in any considerable size, it will be found to overlap the base of the heart and to pass upward, obscuring the shadow, just described, of the great vessels. The shadow of this thymus is again triangular in shape with its base overlapping the base of the heart and especially the auricles." The transverse diameter of the thymus shadow, which is usually the third interspace, may be two or three times the diameter of the shadow cast by the thoracic spine. If the shadow of the thymus is no greater than that cast by the great vessels, it is a small thymus. Owing to the consistency and location of the thymus, it can only spread laterally and downward. "The anteroposterior diameter of the thymus is that of the distance between the tracheal shadow and that of the manubrium and sternum." This shadow blends with the mediastinum. The superior vena cava or a prominent pulmonary artery may be mistaken for the left lobe of the thymus. "Enlarged mediastinal glands should be recognized either by the character of their shadows, or by the associated pathologic change at the hilum of either lung." The exposure is one-twentieth of a second in the recumbent position at full inspiration. The thymus cannot grow anteriorly or posteriorly except under unusual conditions. The size of the gland varies,

not only in different infants, but also at different times in the same infant. In many infants the thymus was small at birth, grew until the age of from 10 to 14 months and gradually receded until the infant was from 28 to 32 months of age, when the mediastinum was no longer broadened and the gland became small.

The author's classification based on size is: (1) those which do not increase the transverse diameter of the mediastinal shadow; (2) those which are twice the diameter of the body of the thoracic vertebra at the second or third interspace; (3) those which are three or more times the width of the thoracic vertebra, or the large thymus. Underweight children are likely to have a small thymus and overweight children a large thymus. Therefore, roentgen-ray examination is especially indicated in overweight children. As the thymus varies from time to time, the examination should be made immediately before operation. The author personally fears operation on children over 2 years of age who have large thymus glands. He recommends roentgen-ray treatment if the children are over 2 years of age. If they are under 2 years, this should be done only when an operation is contemplated, or when the infant has symptoms referable to the thymus.

HUNTER, Philadelphia.

CONNOTATION OF CONSTITUTIONAL PSYCHOPATHIC INFERIORITY WITHOUT PSYCHOSIS. J. H. HUDDLESON, J. A. M. A. **86**:1960 (June 26) 1926.

About 7 per cent of the case histories in the neuropsychiatric outpatient department of Veterans' Hospital 81 reveal a diagnosis of constitutional psychopathic inferiority or some synonymous term made once or oftener during the past six years by the psychiatrists of the Veterans' Bureau or the United States Public Health Service. The observations in a series of 500 cases are presented by Huddleson with the purpose of determining by what diagnostic criteria the conclusion of the presence of a constitutional psychopathic state is adducible.

Following a discussion of the confusion of terms for such cases, Huddleson presents a table of classes of characteristics and individual characteristics with the actual number of cases of each and the percentage.

Of physical manifestations, Huddleson finds anatomic stigmas noted in 8 per cent, although probably too little attention was paid to these; sexual anomalies, including perversion, were present in 4 per cent; enuresis (after the age of 5 years) was present in 2 per cent; onychophagia in 45 per cent; stuttering and stammering claimed 9 per cent. There was addiction to drugs in 1.5 per cent, to alcohol in 10 per cent and excessive addiction to tobacco in 2 per cent. Under traits suggesting a manic-depressive make-up one finds emotional instability in 63.5 per cent. Grandiosity and excessive self-esteem, as traits suggesting manic and paranoid tendencies, are present in 20.5 per cent, while paranoid personality, suggesting a paranoid trend is present in 18 per cent. Metatopomania, polypraxia and employment at occupations beneath the mental capacity are present in 19.5, 48 and 2 per cent, respectively, and are traits suggesting a schizophrenic make-up. Poor cooperation and refractoriness, unreliability (excluding exaggeration and malingering) and conscious exaggeration of symptoms give 36, 31.5 and 41.5 per cent, and are suggestive of mental deficiency. Malingering (charged as such) malingering suspected, truancy and "A. W. O. L." tendency, trouble making and all conduct disorders (including the ones described above) as indicating conduct disorders are present in 5.5, 2, 15, 19 and 50 per cent of the cases.

Huddleson presents three cases in illustration of the more commonly found characteristics. He concludes that: (1) these 500 diagnoses of constitutional psychopathic inferiority and constitutional psychopathic states by thirty-three neuropsychiatrists have been based on a number of accepted symptoms, emotional instability being the most frequent; (2) the diagnosis of constitutional psychopathic state is unsound unless it is a fundamental attribute; (3) constitutional psychopathic inferiority should be considered a symptomatic, not a pathologic, diagnosis, and (4) criminalism should be omitted from the list of constitutional psychopathic states, crime and responsibility being problems too disputed and extensive for its boundaries.

CHAMBERS, Syracuse, N. Y.

CATATONIC PSYCHOSIS WITH MOTILITY DISTURBANCES FOLLOWING CARBON MONOXIDE POISONING. F. KANT, Archiv. für Psychiat. u. Neurol. **78**:365 (Oct.) 1926.

The author discusses the question of catatonic symptom complexes brought about by organic brain disease on the basis of a case of his own, one previously reported by Kraepelin, and gives a review of the literature on the subject. The case is that of a boilermaker, aged 49, who, up to eight months previous to admission was normal. Since that time, owing to the introduction of a new piece of apparatus, he had been subject to slow carbon monoxide effects (as were also some of his co-workers, though not to the same extent), and soon after began to show general symptoms: dizziness, nausea and at times vomiting. During the week preceding admission, he began to show peculiar behavior in the form of periods of mutism alternating with talkativeness and excitement. On admission, he showed marked motor inhibition, a tendency to catalepsy, and mutism. He was depressed. Movements were slow, and the speech was difficult to understand. Psychically, however, the patient did not show any further disturbances. He was taken home; he returned a week later, when he showed stereotyped movements, expressed ideas of reference, and showed mannerisms, catalepsy and echopraxia. He became disturbed and disoriented. Speech was irrelevant and he gradually went into stupor. He seemed to react to auditory and visual hallucinations. Six days later, his condition began to improve, and after a short while he returned to his normal mental state. He had perfect insight but poor memory for events during the stupor. He admitted having had auditory hallucinations which, on further exploration, showed relations to conflicts in his life. Neurologically, he showed absent achilles and patellar reflexes, and a ++ Pandy reaction in the spinal fluid; otherwise the results were negative. The Wassermann reaction was negative. The reflexes returned after three months. The patient returned to his normal condition. No other causes were found to which this disturbance could have been traced.

The case of carbon monoxide poisoning with dementia praecox type of reaction reported by Kraepelin is discussed again, and a report is given of the present condition of the patient; it seems that there, too, catatonic-like disturbances must have been directly related to the effects of the poisoning. The catatonic disturbances in both cases seem to bear a close resemblance to some disturbances of motility in striate body diseases; one must also bear in mind that postmortem observations of carbon monoxide poisoning show disturbances of the basal ganglia.

The author believes that one is dealing in such cases with reversible, chemically conditioned changes, but that in the production of the psychosis the personality of the patient, the complexes and conflicts in his previous experience, play a deciding rôle. One may, however, speculate as to the possibilities of organic components in other types of catatonic psychoses.

MALAMUD, Foxborough, Mass.

CORTICAL TUMORS IN RECKLINGHAUSEN'S DISEASE. EUGEN POLLAK, Arb. a. d. Neurol. Inst. a. d. Wien. Univ. **28**:83 (May) 1926.

Pollak had occasion to examine the brain of a patient who had had Recklinghausen's disease. Except for the usual cutaneous lesions, there were neither clinical nor anatomic evidences of involvement of the central nervous system. The pathologist had apparently overlooked a nodule the size of a large bean in the right parietal lobe. Pollak found the tumor in a convolution, closely attached to the pia and invading the cortex; its surface was irregular and nodular. Although the mass was hard in consistence, it did not have the slightest resemblance to a typical nodule of tuberous sclerosis. Numerous sections of the brain were made, and a thorough search for any other pathologic conditions was fruitless.

Histologic examination of the nodule described showed a peculiar process consisting of a homogeneous center and a neoplastic productive zone at the periphery; it seemed as if the entire nodule was mesenchymatous in nature — it was a process of the supportive tissue that infiltrated ectodermal tissue. Pollak is certain that it was neither a neurinoma nor any other form of ectodermal blastoma, nor a glioma. Although the tumor mass was full of giant cells, he believes that these were derivatives of a mesenchymatous neoplastic process; as far as its mesenchymatous character was concerned, it could be classed neither among the sarcomas nor among the endotheliomas; if anything, it resembled a perithelioma, or perhaps a granuloma, not unlike a tubercle without a caseation of its center. There is no doubt that the tumor was benign; in favor of this was the fact that the blood vessels had a remarkable tendency to regressive metamorphosis. This regressive tendency of the blood vessels in Recklinghausen's disease has also been emphasized by Orzechowski and Nowicki. The presence of so many giant cells is also confirmatory evidence of the relatively benign character of the growth.

From all that has been said, it may generally be concluded that in Recklinghausen's disease there may occur tumors that cannot be definitely identified as neurinomas. This statement is amply borne out by the literature, which contains many reports of cases similar to that (Maas's case) described by Bielschowsky in which a typical neurinoma was found alongside an endothelioma. One must admit that there occur in Recklinghausen's disease tumors which show different tendencies to different forms of growth; these tumors may perhaps be derived from a common source, but their tendency to grow depends on variations in the matrix. This is especially the case with the blastomas.

KESCHNER, New York.

MALARIA TREATMENT OF GENERAL PARESIS. FERRARO and FONG, J. Nerv. & Ment. Dis. **65**:225 (March) 1927.

Two cubic centimeters of blood from a donor was injected into the subscapular tissue, and by this method the period of incubation varied from two to forty-eight days. Intravenous methods show an incubation period of from two to twenty-four days, with an average of five days. Some patients showed an apparently total immunity. The authors feel that when one strain fails, attempts should be made with others. One hundred and twenty patients were successfully inoculated; 25.7 per cent showed good remissions; 27 per cent showed marked improvement, and 8.3 per cent exhibited slight improvement. The total number of deaths was twenty, of which only six died during the acute stage of malaria, placing the mortality rate of treatment at 4.9 per cent.

Demented types showed least improvement, while expansive paranoid types demonstrated the most. Depressed types reacted well—these being the cases that offer the highest percentage of good remissions. Schizoid and juvenile types showed marked resistance to treatment. As for the factor of age, the greatest number of good remissions occurred between 26 and 40 years—the older the patient the less probability of benefit from malaria. Spontaneous remissions from general paralysis, according to various authors, vary from 4 to 17 per cent; in the author's series, 53 per cent showed appreciable remissions. Treatment also seems to prolong life. There is a definite relationship between duration of remission and height of temperature. In these cases, the percentage of serologic improvement increased from the minimum of 15 within the first six months to a maximum of 80 after a period of three years. It was found that the pleocytosis was the first element to improve, with next the globulin and Wassermann reaction; the element most resistive to treatment was the colloidal gold reaction. No parallelism was found between serologic improvement and maximum temperature. Clinical improvement was estimated at 61.2 per cent as compared with a serologic improvement of 36.32 per cent. Neurologic signs, such as pupillary rigidity and inequality, showed slight improvement after malaria, and there were some changes in the deep reflexes. Tremors, defects of speech, incoordination, seizures and ataxia showed varying degrees of betterment, among which the most marked improvement was observed in speech, coordination and tremors. The author believes the temperature is the important spirocheticidal factor in the treatment. Whether any antagonism exists between the malarial and syphilitic organisms is uncertain.

HART, Greenwich, Conn.

GLIOMA IN THE FOURTH VENTRICLE WITH INVOLVEMENT OF THE TRIANGULAR VESTIBULAR NUCLEUS. W. J. SCHALLER, J. Neurol. & Psychopath. 6: 281 (Feb.) 1926.

After an extended discussion of the mechanism of the motor nerve system the author reports a case in a girl, aged 3. The family history is without special interest. The child was apparently well until six months prior to examination when she is reported to have fallen downstairs, but apparently suffered no serious injury. Five weeks later, she began to stagger to the right when walking. Soon after, there was vomiting without relation to ingestion of food, and four months prior to examination she suffered with convulsions which continued for nearly three months. Three months prior to examination, sight began to fail. At the time of the convulsions, she was unable to stand upright, and, soon after, even to sit up; use of the extremities also became increasingly difficult. The sense of taste was involved, and finally, control of the bladder sphincter was lost. On examination at the hospital, the child had a tendency to fall backward when supported in a sitting position. The head was held rigidly at the neck. There was extreme hypertonicity of the muscles of both extended lower extremities. There was moderate adductor spasm. The upper extremities showed flexion of the forearms on the arms and a spontaneous tremor. There was apparently a marked dysmetria in the upper extremities, especially the left. The tendon reflexes were increased, although the responses varied on account of the dystonia. Roentgenograms of the skull showed absorption of the inner table. The pupils were dilated and reacted sluggishly to light. Occasional vertical nystagmus was noted. The optic disks were pale and poorly outlined. The general physical examination and the laboratory tests gave negative results. A diagnosis of probable cerebral tumor

with internal hydrocephalus was made and an operation was performed. The patient died two days later. At necropsy, only the brain was removed and a cerebral tumor filling the fourth ventricle was found. On serial section examination, the left anterior portion of the cerebellum was somewhat more involved than the right. The triangular nucleus was involved in the tumor infiltration. The dentate nucleus was compressed but not involved by the tumor. The nucleus emboliformis and globosus and the inferior vermis were all invaded by the tumor. The histologic diagnosis was: cellular glioma.

POTTER, Akron, O.

NEUROPSYCHIATRIC ASPECTS OF CHOREA IN CHILDREN. F. G. EBAUGH, J. A. M. A. **87**:1083 (Oct. 2) 1926.

Ebaugh stresses the serious neuropsychiatric aspects of chorea in reporting a series of thirty-two cases referred to the outpatient department of the Colorado Psychopathic Hospital. There were eighteen boys and fourteen girls from 6 to 15 years of age, the majority 12 or under. All patients were ambulatory and showed the typical twitchings. The author first considers the mental aspects accompanying or following chorea, such as emotional lability, fatigue and intellectual incoordination, and the relation of chorea to delinquency. Quiet, easily managed children became restless, sensitive, irritable and abusive. Some became violent, and distinctive outbreaks of temper were frequent. Depressive episodes were noted. Some of the children became apathetic, restless and indifferent. Silly, causeless laughter was observed. Insomnia, night terrors and sleep walking were prominent. Ebaugh then reports a typical case with kymographic tracings.

Delinquency occurred in 21.2 per cent of the cases studied, with such offenses as vagrancy, truancy, lying and stealing automobiles. Ebaugh feels that the association of delinquency with chorea is definite and that physical study is important, as delinquency occurs in spite of the best environment. He found positive physical signs in twenty-nine of the thirty-two cases, such as attacks of tonsillitis, dental infection, refractive errors and adenopathy. There is a strong hereditary tendency to chorea (43 per cent in this series), as pointed out by Osler, and Ebaugh presents a diagram to illustrate such a case. Chorea resulting from fright did not show marked frequency of occurrence in the series, toxic as well as psychogenic factors being present as a cause.

The author emphasizes the importance of complete rest and isolation, often in a new environment. All foci of infection should be eliminated. Ebaugh prefers six weekly injections of tryparsamide to Fowler's solution. Sunlight should be accessible; arrangements should be made for short school periods during convalescence, and physical and mental strain should be avoided. Parents should be warned against too much sympathy. There should be definite supervision, fundamental training in habits, and the parents should not show concern before their children. Ebaugh also stresses the continuance of the twitchings as a habit after the cause has been removed.

CHAMBERS, Syracuse, N. Y.

PROGNOSIS IN SCHIZOPHRENIA. EDWARD A. STRECKER and GORDON F. WILLEY, J. Ment. Sc. **73**:300 (Jan.) 1927.

This article is an attack on the idea that the patient who has dementia praecox never recovers. Perhaps this idea is not to be found in a close reading of any textbook of psychiatry, but it is admittedly a powerful one none the less, and

influences unfavorably the treatment of all patients so classed. The clinical limits of schizophrenia are discussed according to the views of Kraepelin, Stransky, Meyer, Bleuler and Kirby. The authors conclude that "the true state of affect probably constitutes the safest index of prognosis," but realize the difficulties in the way of finding out what the real affect is. Their analysis of precipitating situations shows that often an apparently malignant, schizophrenic process may be resolved into benign factors which by their accidental grouping simulate something worse.

Patients were studied who were admitted consecutively to the department for mental and nervous diseases of the Pennsylvania Hospital with the diagnosis of dementia praecox. Of these, thirty-eight recovered and have remained well about five years to date. Several definite considerations in prognosis are raised. Race in immigrant Jews and in isolated Pennsylvania Dutch stock has given to some of these patients a sinister cast which has not been justified. The psychiatrist's lack of understanding of ways of thinking foreign to himself is the cause. Heredity in one case played a deceptive part; the mother's chronic paranoid condition made physicians think the daughter would follow in her footsteps. Closer study revealed that in her psychosis she was showing the influence of training and was copying the mother's symptoms. After a while recovery followed.

The "shut-in" person may be a normal one putting up barriers against an abnormal environment; and catatonic manifestations may mean only stubbornness carried far. If the precipitating situation is important and reflected in the content of the psychosis, the outlook is better. Toxic clouding of consciousness may mask the expression of affect. Altogether the article calls for individualization in the study of the patient, the refusal to allow classification to determine individual prognosis, the careful study of the precipitating situation and the present psychosis.

BOND, Philadelphia.

DIASTATIC ACTIVITY OF THE BLOOD SERUM IN MENTAL DISORDERS. J. W. RAUTH, Studies in Psychology and Psychiatry **1,** no. 2 (June) 1926.

This article gives the results of exhaustive studies of the chemistry of blood serum in various types of psychoses. The observations are checked against cases of pure somatic disease, and controlled by similar studies in normal persons. A thorough review of the literature takes up about half the article and shows considerable lack of uniformity of methods and results in the estimation of blood diastatic activity.

The general principle involved in the determination of diastatic activity of the blood is a measurement of the sugar produced by the action of blood or serum on starch or glycogen and the measurement of the time required to hydrolyze a fixed amount of starch or glycogen by a definite quantity of blood serum; or, the determination of the amount of serum necessary to hydrolyze a fixed amount of starch or glycogen in a given time. The author's method determined the amount of blood serum necessary to change 2 cc. of a 0.1 per cent starch solution to dextrin in thirty minutes at 38 C. From several tables, he draws the following conclusions: 1. There is no marked difference between the average values for normal persons and patients with dementia praecox. 2. There is no marked difference for cases diagnosed involutional depression. 3. The miscellaneous group of psychoses show no marked difference from the normal group. 4. The manic-depressive group show on the whole a higher d (diastatic unit) as compared with the normal group.

The increase in diastatic activity in manic-depressive psychoses is apparently linked with a lowered renal function, and places the disease somewhat in the somatic group. In support of this idea, the author quotes from unpublished data, obtained from Dr. G. C. Kirk of St. Elizabeth's Hospital, tending to show that the necropsy diagnoses demonstrate a higher death rate from nephritis in the manic-depressive than in any other group. The author states that values as high as 18 d (normal being 12.3) usually indicate a manic-depressive psychosis, and in his group 4, this class showed an average of 16 d. These observations would, in a manner, offer a therapeutic aid in the treatment of the manic-depressive psychoses.

PATTEN, Philadelphia.

MENINGITIS CARCINOMATOSA. T. G. MOOREHEAD and T. J. WIGHAM, Irish J. M. Sc. **3**:135 (March) 1926.

The authors report the following case: a man, aged 42, complained of pain in the head, vomiting and dysphagia. Examination showed rigidity of the neck, a positive Kernig sign, a positive Brudzinski sign, absent knee jerks and no nystagmus or optic neuritis. The spinal fluid, which was under greatly increased pressure, showed an increased cell count, a negative Wassermann reaction, and absence of sugar. The vomiting continued. Punctures every second day were necessary to relieve pain in the head. Death occurred October 1. A provisional diagnosis was serous meningitis,. At necropsy, 'the brain showed no gross changes except slight thickening of the pia-arachnoid. Microscopic examination of sections disclosed a tumor growth of endothelial cells in the pia over the entire cerebrum and cerebellum. In places in which the growth was more in evidence, there was a definite tendency to the formation of tubules lined with a single layer of cells. The histologic diagnosis was endothelioma.

POTTER, Akron, O.

VERTIGO. ITS INCIDENCE IN ENDOCRINE DISORDERS. DANA W. DRURY, J. A. M. A. **87**:26 (July 3) 1926.

Following a brief discussion of the physiology of equilibrium and vertigo, Drury presents a tabular analysis of 1,100 consecutive cases which presented stigmas of possible endocrine disease. Sixty-six per cent gave sufficient evidence to warrant a diagnosis of endocrine malfunction, while 34 per cent presented a primary pathologic condition which was not endocrine. In the endocrine group is an incidence of vertigo of 14.9 per cent; in the nonendocrine group, 20.2 per cent. Cases presenting a pituitary, a thyroid, a cardiorenal and a psychoneurotic type are presented. Drury concluded that: vertigo is an aural symptom; the eighth nerve, rather invulnerable from without, seems susceptible to toxic agents from the blood or lymph streams; vertigo in young persons is usually transient and unimportant, while in elderly people it is apt to be recurrent and of serious import; the only endocrine connection is through a lowered vital function.

CHAMBERS, Syracuse, N. Y.

CONTRACTURED ULNAR PARALYSIS RELIEVED BY TREATMENT OF THE NASAL (SPHENOPALATINE) GANGLION. W. R. BRANDON, Arch. Otolaryng. **4**:493 (Dec.) 1926.

The patient complained of severe pain in the left side of the head and neck extending down through the left shoulder, arm and hand, which resulted in a contraction of the ring and little fingers, severe enough to cause excoriation in the palm of the hand. At times there was pain in the left leg. The slightest effort to extend the fingers produced excruciating pain. The nose showed

hyperplastic thickening but no pus. The application of cocaine to the ganglion area was immediately followed by relief of the headache. Two days later, the man still complained of some pain; so the treatment was repeated and was followed by the application of 2 per cent silver nitrate. This treatment was continued for six weeks. At the end of three months, there was enough relaxation to allow the fingers to extend to about half the normal degree. The condition continued to improve and finally cleared up entirely.

HUNTER, Philadelphia.

LEAD POISONING IN NURSING INFANTS: REPORT OF TWO CASES DUE TO THE USE OF LEAD NIPPLE SHIELDS. HERBERT B. WILCOX and JOHN R. CAFFERY, J. A. M. A. **86**:1514 (May 15) 1926.

A short review of the literature on lead poisoning is followed by reports of two cases both of which were the result of the use of lead nipple shields, a source not previously reported. In both cases neurologic symptoms developed. The patient in case 1 still has marked anemia but no nervous or mental symptoms. In case 2, the patient was slightly irritable after six weeks. Anemia persisted in case 1, but the child improved greatly and gained weight under treatment. The authors believe that the use of lead shields for two or three weeks does no harm, but that after that they should be discontinued and other measures of treatment of the diseased nipples instituted.

CHAMBERS, Syracuse, N. Y.

SECTION OF THE SUPRARENAL NERVES AND ITS EFFECT ON THE ORGANISM. A. CIMINATA, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **28**:95 (May) 1926.

Ciminata performed bilateral section of the branches from the celiac ganglion as well as from the major and minor splanchnic nerves to the suprarenals in cats and dogs. Following this operation the animals remained alive and in good condition (the longest period of observation was three months). The effect of the operation on the animals' capacity to develop convulsions could not be determined. The increase in the blood sugar induced by painful stimuli was much lower in animals subjected to the operation than in normal animals. Bilateral section of the suprarenal nerves was followed only by a slight reduction in the animals' epinephrine output, but the excretion of this substance into the circulation was definitely disturbed.

KESCHNER, New York.

THE SUGAR AND CHLORIDE CONTENT OF THE CEREBROSPINAL FLUID WITH SPECIAL REFERENCE TO NEUROSYPHILIS. S. W. BECKER, Am. J. Syph. **11**:37, 1927.

Using the Rothberg-Evans modification of the Folin-Wu method for sugar determination, the author finds a definite, though small, decrease in the reducing substances of the spinal fluid in cases of neurosyphilis. There is also a slight normal variation in normal sugar content values, but not of such range as exists in the blood. There is a slight tendency toward low sugar values with high cell count and in cases showing the colloidal benzoin reaction in the first zone. No alteration occurred in patients undergoing treatment for as long as five months; nor did an alimentary glycemia up to 185 mg. per hundred cubic centimeters produce an increase. A slight normal variation in the chlorides was found, less in quantity than in the blood; no changes were demonstrated in neurosyphilitic cases.

ANDERSON, Philadelphia.

THE EFFECTS OF AN EXCLUSIVE, LONG-CONTINUED MEAT DIET. CLARENCE W. LIEB, J. A. M. A. **87**:25 (July 3) 1926.

This paper deals with the history, experiences and a clinical survey of Vilhjalmur Stefansson, Arctic explorer. Lieb points out that: (1) Stefansson spent eleven and one-half years within the Arctic circle; (2) he lived for a total of nine years on an exclusive meat diet; (3) he lived for nine successive months on such a diet; (4) he reached his maximum weight while subsisting on meat (fish); (5) his sense of physical and mental well being was at its best during that period; (6) this diet was as effective whether he was active or inactive, and in warm or cold weather; (7) he was never constipated; (8) his hair thickened and his scalp became healthier; (9) tooth decay was much slower.

CHAMBERS, Syracuse, N. Y.

THE USE OF TRYPARSAMIDE IN NEUROSYPHILIS. S. I. SCHWAB and L. D. CADY, Am. J. Syph. **11**:1, 1927.

Two hundred and thirty patients with neurosyphilis received from one to nine courses of tryparsamide consisting of from six to ten injections at from seven to fourteen day intervals. Various mercurials and arsenicals were used concurrently. The authors state that the tryparsamide method has proved superior in their hands to other approved procedures, yielding clinical improvement or arrest in 78 per cent of the general paralytic patients (sixty-three cases of general paralysis in the series). In the main, these were not institutional cases. A resumé of the literature dealing with malarial treatment of general paralysis is included.

ANDERSON, Philadelphia.

RETROBULBAR NEURITIS IN DIABETES. S. M. FRANCIS and IVAN KOENIG, J. A. M. A. **87**:1373 (Oct. 23) 1926.

The authors conclude that: (1) glycosuric amblyopia is a clinical entity, the result of an endogenous toxin; (2) the precise toxin or toxins cannot be specified but are related to the ketone bodies especially acetone in the urine; (3) glycosuric amblyopia is more common than the literature indicates, and (4) routine studies of the central field should be made in all diabetic patients complaining of visual disturbances. They also report a case and discuss the literature.

CHAMBERS, Syracuse, N. Y.

LEVULOSE TOLERANCE TEST IN PARALYSIS AGITANS. E. W. HURST, J. Neurol. & Psychopath. **6**:291 (Feb.) 1926.

The author reports in detail the results of sugar tolerance tests in eighteen cases of paralysis agitans, five normal persons and four patients suffering with cerebral vascular disease; he concludes that, while there is inconstant hyperglycemia in paralysis agitans, this is present to a similar degree in cases with cerebral vascular disease; hence, the levulose tolerance test is without value in the diagnosis of paralysis agitans.

POTTER, Akron, O.

EROSION OF THE PETROUS BONE BY ACOUSTIC NERVE TUMOR. DEMONSTRATION BY ROENTGEN RAY. E. B. TOWNE, Arch. Otolaryng. **4**:515 (Dec.) 1926.

Roentgenograms were taken with the head extended with the center of the film under the foramen magnum and the central ray directed through the midline of the frontal region. The author urges that this roentgen-ray technic be used

to make early diagnosis when only auditory symptoms are present and when surgical procedures could be much less extensive. Three cases are quoted in which the technic demonstrated acoustic tumors.

HUNTER, Philadelphia.

THE RACIAL PROSPECT OF GENERAL PARALYSIS. LEO KANNER, Am. J. Syph. **11**: 23, 1927.

This is an interesting review of the incidence of general paralysis among different races. Some explanation of the variability noted is made on the theory that it requires some two to three centuries after syphilitic infection of a nation before general paralysis makes its appearance. There follows a progressive increase for some two centuries and finally a gradual subsidence in the number of cases.

ANDERSON, Philadelphia.

A STUDY OF SUBJECT MATTER AND MOTIVATION OF CHILDREN'S DREAMS. PHYLLIS BLANCHARD, J. Abnorm. Psychol. **21**:24 (April) 1926.

This is a tabulated statement of the physical and mental condition of 189 children who recalled their dreams, the age at which they occurred, and the type of subjects of the dreams. Forty-six per cent were classed as wish fulfilments and 40 per cent were related to fear. It is realized that dreams of children may be of real clinical assistance in coming to an understanding of the child's difficulties and general psychology.

HAMILL, Chicago.

"HOOCH," "HOME BREW," AND COPPER. EDITORIAL, J. A. M. A. **86**:1552 (May 15) 1926.

Copper, because of the advent of the bootlegger, has joined the ranks of lead, mercury, zinc, arsenic, carbon monoxide, methyl alcohol and war gases to worry the peaceful citizen. While it is a useful metal, it should not be employed when it comes in contact with foods and drinks, particularly those containing acid.

CHAMBERS, Syracuse, N. Y.

EPILEPSY IN CHILDHOOD. M. G. PETERMAN, Am. J. Dis. Child. **32**:416 (Sept.) 1926.

This article is an excellent critical review of the recent literature of epilepsy with particular reference to the disease as found in childhood. The data are grouped under the headings of heredity, etiology, diagnosis and treatment.

VONDERAHE, Cincinnati.

SEX IN TANTRUS. K. C. MUKHERJEE, J. Abnorm. Psychol. **21**:65 (April) 1926.

This article would give a much clearer picture to a reader versed in the terminology of the Brahmin hierarchy. However, it is apparent that energy or libido, or impulse, is thought of as arising from sexual sources.

HAMILL, Chicago.

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A CASE OF PITUITARY TUMOR WITH COMA FOLLOWED BY COMPLETE RECOVERY. DR. IRVING J. SANDS.

A tailor, aged 57, began to lose his eyesight in the latter part of 1921. The condition was recognized as one of pituitary tumor, but it was decided that it was too late to operate. Pituitary extract was prescribed, and the patient was permitted to return home. His son learned to recognize by the change in his personality when he needed pituitary extract, and it had been given persistently.

On July 11, 1926, he had a headache, began to vomit and was irritable; on the evening of July 13, he became restless. His son, a physician, gave him one-fourth grain (0.016 Gm.) of morphine. He became comatose, and had definite Cheyne-Stokes respiration.

On July 14, 1926, when first seen, the patient was in coma. He had irregular, sluggish pupils. The left optic nerve was definitely atrophied; the right showed atrophy of the temporal half. He was admitted to the hospital, and a lumbar puncture was made. There were: bilateral signs in the pyramidal tract; blood sugar, 149 mg.; urea nitrogen, 5.8; and creatinine, 1.77 mg. per hundred cubic centimeters. Abdominal reflexes were absent. There was sugar in the urine. After the lumbar puncture, surgical pituitary extract was administered, one ampule every three hours for three days and then one ampule every four hours.

Within thirty-six hours the man regained consciousness, and the pyramidal tract signs disappeared. He was able to talk distinctly. Vision in the right eye was limited to the nasal half of the field. The roentgenogram of the sella showed that the clinoid processes had disappeared. The floor of the sella was depressed. There were evidences of mixed hypopituitarism and hyperpituitarism, with scanty hair and the contour of body peculiar to the pituitary condition. The right eye turned slightly to the right, because it permitted him a larger field of vision. The patient received surgical pituitary extract, 1 cc. a day, and sometimes every second day. The son recognized that it was needed by the extreme irritability, headache and at times vomiting. Occasionally a lumbar puncture was performed. Sometimes thyroid extract was added to the pituitary extract. There was a little elevation of the blood sugar curve. The patient made no complaints. He was able to care for his son's office and answer the telephone; intelligence was intact. Polyuria was not present.

DISCUSSION

DR. J. H. LEINER: A number of questions present themselves. What happened at the time of the lumbar tap? Is it possible that the neoplasm was of a cystic type, which was relieved by this procedure? Relative to the blood

sugar, water metabolism and the administration of pituitary extract, there is considerable controversy. Are the first two functions based on a purely glandular or neurogenic origin or on a combination of the two? One school, led by Camus and Roussy, believes that it is due solely to neurogenic control. This patient had a pituitary syndrome concomitant with coma. Was this a real coma? It is not borne out by retention in the blood. This center has often been referred to as the hibernating region. Was not this, therefore, an allied state rather than a true coma? How much vision returned? How long does Dr. Sands believe he can maintain the administration of pituitary extract.

Dr. Sands: The neoplastic pituitary gland was probably inefficient in furnishing the pituitary extract required for metabolism. That has been supplied by the administration of surgical pituitary extract. I felt that, immediately preceding the coma, a demand was made on the pituitary gland to furnish its secretion. This demand was naturally accompanied by engorgement of the neoplastic pituitary gland, causing pressure on the iter, which resulted in increased intracranial pressure and may have been a factor in producing the coma. I removed 75 cc. of fluid, hoping that it would relieve the intracranial pressure, which it apparently did. I ordered the administration of surgical pituitary extract, hoping that this procedure would remove the load from the neoplastic pituitary gland. Morever, for a period of about five years pituitary extract had been given in the same manner, with good results. The urea and creatinine content of the blood may be said to be normal. The sugar content is higher than normal, and there has occasionally been sugar in the urine. I believe life will be prolonged for many years by giving pituitary extract.

An Analytic Study of Stereotyped Habit Movements in Children. Dr. L. Pierce Clark.

If it were not for the late effects on the evolution of habit formations, and especially the motor reactions, the persistence of head rolling, head banging and similar disorders of motility in childhood would probably be annoying only to members of the households in which these children are reared. Although these stereotyped movements are classed with disorders of sleep, they have no connection with the latter except in time relationship. Indeed, sleep is often disturbed but slightly. The auto-erotic character of the movements is at once suggested by their regularity and by the reproductive ceremonial. In the unconscious the movements serve a pleasurable purpose which is not often entirely discarded by the subject's conscious desires, and the children often assume positions in sleep favorable for the act.

The intensity and persistence of the habit range from a deep unconscious motivation to simpler types of purposive movements, which are partly controlled by rewards or discipline, to the type whose motivation is deeply buried in the unconscious.

From an objective standpoint, inquiry into the nature and causation of stereotyped habit movements in children brings up the initial types of movements in infants. The first are peculiar, wormlike movements of stretching, pulling and turning, possessing many of the types of segmental movements as seen or known to occur in the fetus. In earliest infancy the child pulls and tugs with its fingers, often hitting itself in an aimless fashion, as seen in the bath, on waking and sometimes on going to sleep; in the latter state the movements are usually slow, and come to an arrest as though they were finally blocked or retarded before the full movements were accomplished. These

earliest movements are called impulsive. They endure more or less characteristically throughout the first year of infancy. They are seemingly repressed or replaced by other types of movement consonant with the adaption of the growing organism to its environment. These impulsive movements have no relationship to reality as adults know it. They are apparently a survival of the intra-uterine life. If for some reason the repressing forces of development do not operate, the ideational and imitative movements fail to succeed them, and they persist in an age of development in which they serve no adaptive purpose. The later types of movement, repressed by effort of the will and otherwise, occur during sleep when conscious control is at a minimum. Even in going into and waking from sleep these impulsive movements persist in all animals, including the human being. While the movements from their intra-uterine inception are slow and wavelike, they are capable of taking on all the characteristic deviations in type drawn from all the neuromuscular patterns of infantile behaviors. In some instances, in spite of the rather superficial and illogical method of repressing the more benign types of motility disorders of infancy, one is able by training of the will to succeed in repressing them acceptably. The egotistic dominance often prevents these children from making a satisfactory adaptation to environment. They daydream and are filled with idealistic and fanciful wishes of motor or muscular erotism.

The child's attitude toward the habit varies from a sly, secretive encouragement of the act to an apparent obliviousness that he is doing it and a sincere, conscious desire to be rid of the disorder. This double motivation of desire is often seen and may vary from one attitude to the other; in other words, the response is not dissimilar to that governing other neuroses, and especially that of the ticqueur, who suffers from the somatic narcissistic neurosis par excellence.

Case 1.—A boy, aged 6 when first seen, at the age of 3 months had had a tendency toward a rhythmic to-and-fro movement in the daytime. Soon this habit was dropped, and he began rolling his head, his arms held in the air, and oscillating from side to side. This movement persisted in sleep despite attempts to break the habit. All sorts of disciplinary measures were taken to suppress the habit, but little improvement resulted. He developed slowly as to physique and held his place in intellectual development. No particular treatment was followed, and at the present time, in his seventeenth year, his schoolmates observe that he indulges in the habit occasionally.

Case 2.—A boy, aged 7, when first seen, since the age of 8 months had had a habit of bumping his head at night, turning on his abdomen, raising his head high, then relaxing and letting it drop on his arm, which he held in such a position that the forehead struck the forearm. If allowed to do as he wished he would repeat the bumping in perfect rhythm ninety times without stopping. This boy, like the one in the previous case, was given no special treatment. He is now 19 years old, physically robust, a good athlete, and has just finished the first year at college. There are practically no nervous mannerisms except that he appears to be rather high-strung. It is evident that without much suggestion he succeeded in sublimating his auto-erotic muscular activities into athletics, so that his egoistic satisfactions may be said to have been met by socially acceptable ends.

Within the past four years I have had occasion to study two cases psychanalytically.

Case 3.—J. L., when first seen was 14 years old and was up to his age, both physically and mentally. For a year and a half before coming under observation he had had a habit of swaying his head and arms, grimacing and making clucking sounds. The movements ceased in sleep, and were indulged in unconsciously during the waking state; they were rhythmic and slow. Unfortunately, the parents discontinued the treatment after one month. From the material gained in the short analysis, it was found that the main factor was unsuccessful repression of a homosexual trend directed toward an uncle. This trend in turn was conditioned on his incomplete weaning from the breast. The slow movement of the head was found to be not dissimilar to the groping action of the infant seeking the breast. The ego continually regressed to different levels until it gained a respite from the homosexual conflict, and in the process of analysis he showed all different degrees and depths of regression. These were sublimated in the reverse order from that ordinarily seen, for as he went back to the egoistic trends and made a heterosexual projection, he broke away from the homosexual attachment to the uncle. There was also a corresponding ability to project the libido in the direction of an object choice. When he made a definite transference to the analyst, he gradually lost the habit movement. At present, one year after he was first seen, he has discarded the larger movements; he still shakes his head occasionally when at home, but his teachers state that they have not noticed it in class.

Case 4.—In a boy, aged 12, of the neurotic type in which the endowment of primary narcissism of intra-uterine life (impulsive movements) was initially at fault, these defects or traumas were reinvoked again and again by the successive defects of life adaptation. In other words, several castrations or weanings brought to light confirmed the continuance of the head rolling in spite of all training the parents could bring to bear. The profound organismic importance of these muscular (erotic) movements shows how absurd and superficial is the attempt to attribute their origin to imitation. These so-called habits are only invoked by the later precipitants, which are not their real cause. It is interesting to see how in all probability the initial erotic fixation (or imperfect libido upbinding) prevents the normal development of these muscular activities to pass to their respective goals of later sublimination, or to be discharged off or out at their succesive levels of organismic use. These fixations also entail widely remote handicaps of a psychic and social nature. The latter in turn make for compensatory or reaction formations against the castration effects of the handicaps that are puzzling in interpretation, if one fails to consider the widely pervasive effect such a primitive error entails. Although the analytic data obtained are inconclusive, they steadily point to the wealth of material brought to light for continued study and to the importance of realizing that without a better knowledge of the as yet vague evolutions of mind in the infant one will not be able to understand the neuroses of the pregenital period.

To schematize the analytic inquiry of four months' duration in case 4, which may also serve as a summary, this boy has in great part given up the intensive aspects of the head rolling habit, but under conditions of stress, fatigue, insufficient sleep and return to the exciting family relations (there are four boys in the family, all inclined to highly exciting activities) the head rolling and extra-physical activities return. Secondarily, the head rolling is analogous to the intra-uterine movements, which probably are part of the excessive primary narcissistic endowment in the functioning of the several organs in their organismic unity. These movements are reinvoked at each

level of successive periods of adaptation, and may be added to in proportion as there is an insufficiency of ego libido cathexis. The libido flows back, and attaches itself to the primary inadequacy and fixation of impulsive movements of intra-uterine inception. The necessity for a prolonged collateral investigation of the withdrawal of libidinal values out of every sort of childish objectification of interest is well shown in this boy. Like all purely objective and descriptive phases, however, this fails to give the deeper and genetic instinctive value of the whole process, which the incomplete and brief analysis here has shown to be rooted deeply in the whole viability and the utility by which different kinds of voluntary and involuntary functionings of the organism can be used for auto-erotic purposes.

DISCUSSION

DR. J. H. LEINER: According to the work of Meige, Feindel and others, a person who is subject to tics and allied movements is a born ticqueur and always remains such. Cured of one movement, he acquires another. That has been shown clinically in extensive studies by the French school. I have a patient who was treated according to the old Bernheim-Nancy school, fifteen years ago. He was an embroidery worker who developed a severe tic, involving not only the eyes, which rolled around their axes, but also affected the risorius muscles, so that he resembled Victor Hugo's "l'homme qui rit." Under hypnosis these movements disappeared after one or two seances. Seven years later, he returned with peculiar jerking and ticlike movements involving the lower extremities. These again disappeared with hypnosis. I have not seen him since. No matter what type of therapy is used, the question remains, are these patients really cured and do they remain cured?

DR. MORRIS GROSSMAN: The type of tics which I have been accustomed to handle is somewhat different and more or less acquired. I have not used analytic methods. I believe, with Dr. Leiner, that while these tics may be of psychogenic origin, they do not necessarily require analysis. The method I have used is a combination of the reeducational methods outlined by Brissaud with Oppenheim's method of inhibition. I have secured fair results that have persisted for a considerable time. They require, however, prolonged treatment, and close cooperation from the patient and his family. While a tic can be displaced and perhaps cured, unless these patients are kept continually under observation and direction, the results are usually replacements from one location to another.

DR. CLARK: It has unfortunately turned out as I feared when I presented this brief abstract of my studies on stereotyped habit movements in children; the essential contention of the paper has been misunderstood. The paper deals with habit movements of children and not with tics, however closely allied in genetic origin the two disorders may appear to be. The first two cases exemplify the milder types and how they may be successfully handled with care and continued training in self mastery; the last two patients were intractable to all training and only after a specific analysis was undertaken was it possible to modify favorably the enduring head rolling habit. Not only did analysis prove of therapeutic worth, but it gave a deeper view of the intricate nature of the psychologic formation of libidinal habits aggregated about the development of muscular movements. The greatest value, perhaps, is a knowledge of the manner in which erotic absorption of the libidinal release at more primitive levels takes place. Unless one can see the later improvement, one may not say that the disorder is on the way to permanent elimination.

PREVENTION OF NEUROSES. DR. ALFRED ADLER, Vienna, Austria.

The main goal of every school in medicine is to understand and to develop its understanding so that undesirable situations may be prevented. And so my view is directed toward finding out the situation and the possibilities for preventing neuroses. My views are directed toward the education of the child. Since education has become a science, the type of life of the child, the basis of his whole development, is fixed and accomplished in the first years; all schools agree with this. Therefore, it would mean much progress to find the means to construct and establish this basis in such a way that all future events of life could not change the child, and could not damage it so that it becomes neurotic. This consideration applies not only to neurotic persons, but also to "problem children" and to criminals. In these classes one can always find a lack by going back to the beginning of life. Individual psychology is interested in trying to find the way to overcome difficulties, to achieve a goal, the goal of superiority, in which a child can foresee a certain degree of security, happiness and superiority. In general, all life is a striving to overcome difficulties and to develop a totality. Certain types of persons develop on the basis of a feeling of inferiority, and therefore they are always occupied in developing personal superiority in other ways. In all those persons the greatest striving is for superiority. They are always occupied with themselves more than with others; these children feel as though they were in a strange country—not equal, always suppressed; they are, therefore, egoistic and selfish. It is as though they did not have time to be interested in others; if you look closely enough, you will see that they never had any contact with society. They had at most a contact with one person, as a rule, the mother. It is therefore understandable that they have certain characteristics, which I call neurotic characteristics; they are always looking more for personal superiority and are not interested in society; in this way they lack some important virtues. They avoid every change in life, because they are anxious not to be defeated; they try always to retain old situations. Out of such behavior and attitudes hesitation develops. All new situations in life involve social situations; school, occupation, love and marriage, all are social contacts. These persons are lacking in social feeling.

To illustrate with a case: A girl was for three years the only child and the center of the family. A sister was born and created a new situation. Because the older girl was spoiled, she was not prepared for this new situation. She had a feeling of being dethroned; she must begin to fight. Therefore she was always fighting and became an aggressive and attacking child. The younger sister was spoiled because she was little and weak; her development was slow, and she became the center of the family. The younger child was held up as an example to the older. In the great hopes for the second spoiled child the same mistake was made as with the older. The second child could not stand new situations, especially in school. She had never developed a fighting attitude; she had not had to learn it. She never finished anything; never accomplished anything; she developed a hesitating attitude, and the older she grew, the more this hesitation increased. It was obvious in questions of occupation. She played the piano well but was not satisfied because another pupil played better; therefore she gave it up. She could not get dressed in time; she could not be on time to take a walk; everybody must wait for her. In this way she felt herself the center of the house. The older sister married early; the younger hesitated and was unmarried at 30. There is the same trend, the same hesitation.

You can guess the choice of such a girl for a husband. To be sure of being the center of attention she chose a man suffering from tuberculosis, in a weak condition. The parents objected, and the man died. She complained for some years, and then married a man twenty years her senior. She married into a situation in which she could expect to be the center of attraction. The man was happy to marry her but could not always appear inferior and spoil her. He wanted also to be appreciated. This he was always expecting and never achieved. She was interested only in her own person. Her housekeeping was poor; she soon became pregnant, and had a child. In her conjugal duties she, like many women, could not find the goal of superiority; she regarded it as showing the superiority of the man, and therefore avoided it. One can see that the whole sexuality of such a woman must agree with her goal in life. As the sexuality did not lead her to feel herself the center, she avoided the relationship. She began to be excessively clean and pure; she avoided sex relations. The best means she could find to avoid a second pregnancy was always to be washing. Women with such a wish-compulsion are judging and sentencing the whole world. It is almost like committing suicide, but so far this woman did not go. She had a connection in life, because she had the child, and she had the ambition not to lose this marriage. She would rather have been divorced, but ambition did not permit, and she must remain married, although she hindered every consequence of it. She found another excuse to avoid her husband; she began to pray, and her prayers lasted for hours. If she was disturbed she had to go back and begin all over again, so that these two weapons had the same result; the husband was excluded.

If you agree with me that the mistake was made in childhood, and if the means to prevent such a development is sought, where must one look? The answer must be, in the past; the parents must have made the mistake. The parents of today are not well able to provide the remedy. The family with its great advantages (and I can think of no other institution to replace the family) has some disadvantages. I do not believe that the family is able to give a child the great qualities of independence, of courage and of social feeling that are needed for the prevention of neuroses. Parents cannot do this; physicians do what they can, but they cannot prevent, because it is always patients who are the products of these conditions whom they see and treat. What can be done in this way? The answer is, I believe, simple. The possibilities and facilities of the school must be built up and increased. The prevention of neuroses, of "problem children" and of criminality can be accomplished only in school by teachers. That is the only point at which the question can be approached. This, I believe, is a great field for physicians: to teach teachers, to show them how to recognize whether a child has the right development, the right attitude toward life, for facing its problems. These problems are always social problems; they are always problems in which the child must see that he is working on the useful side; it means that the child must have sufficient courage and independence and self-confidence. I have been working with teachers for fourteen years. Since teachers understand the attitude of children toward life, since they understand how to change these attitudes and to give courage, it influences also the parents and the environment. To prevent neuroses, physicians must join with the schools; physicians have great power and means in New York, and great results could be accomplished.

DISCUSSION

DR. L. PIERCE CLARK: The type of neurosis which Dr. Adler excellently presents is well known in the clinic, in school and in private practice. What I dis-

tinctly take exception to is his indictment of the environment as an explanation for such disorders. This was long the practice both here and abroad; but on further and deeper examination one finds a train of inner conflicts that offer a much better genetic and psychanalytic interpretation than that which Dr. Adler draws from parental and social neglect. The latter contributes, but I deny that such explanations are fully causative. His prevention is still the old disciplinary principle brought forward in a new dress. Again, his type of ego neurosis is but one of many and even large types of neurotic disorders in children. Time forbids even a short clinical description of these shy, timid and nonassertive types of neurotic children. Disciplinary measures, even with his special type, fail after a while when the child's strategy and chicanery enable him to circumvent the various authorities of teachers, social workers and parents. Children with antisocial tendencies have long been given over to an analytic understanding of their inner conflicts, and their latent instincts have been allowed to work for inner and not outer circumvention as Dr. Adler contends. When he says that he can work a lasting change by the method which he has outlined this evening, I can only say that, strive as one may, efforts by his lines of therapy have not been attended by such results. Happily, physicians are steadily giving up such outworn concepts of the essential faults in the neurotic child, and are obtaining better results.

Dr. Israel Strauss: I enjoyed Dr. Adler's address. In listening to him, I gathered that he did not attempt to describe the various forms of neuroses which one finds either in childhood or in adult life. I inferred that he used one class of neuroses as an example. I believe, as Dr. Clark has said, that neuroses are not recognized in many cases either by parents or teachers in the early life of the child. When they make themselves manifest, either in difficulties or in asocial adjustment, that manifestation appears in adolescence or later, so that it would have been impossible to handle that person at the period of early school life. But, of course, in cases of neurotic children, in whom disturbances in behavior and conduct appear early, I believe that Dr. Adler is correct in saying that the school should recognize these conditions and attempt to correct them as soon as possible. In order to do that it would be necessary, it seems to me, not merely to have the social worker, but to have the teaching force, which is instructed in modern psychologic methods and knowledge, instructed more in the use of the terminology of either Freud or Adler. As I meet teachers and others who deal with education in the primary schools, I find that they can use the word "complex" and "inferiority" glibly. But what they mean by them they have often not the slightest idea. To carry out a scheme such as Dr. Adler proposes, the teaching force must be educated. I would not say that the teachers in the higher grades are always better prepared and more intelligent than those in the lower grades, and yet they are supposed to be. I think that is a mistake in the educational system. The teachers who are best trained and most intelligent ought to be in the lower grades.

In speaking of the development of the neuroses in this case, Dr. Adler spoke of the fact that a child, aged 3, was surprised in its position of security by the advent of a rival. This happens in many families. The period of latency is somewhat uniform in modern civilization. It must be admitted that those children become the center of attention on the part of the parents and probably are spoiled, if by spoiling you mean that everything is done for them that can be done. Every family that has such a situation certainly does not find that the child of 3 develops antagonism to the succeeding children, nor that it feels itself

compelled to assert a superiority. What bothers me in this psychologic attitude is that there is something in such a child as the one described by Dr. Adler that compels it to have recourse to methods and means to satisfy itself so that it does not become neurotic. In other words, if I describe a case of pneumonia and tell you the symptoms, both subjective and objective, it would not satisfy you; you would want to know the cause of the pneumonia, and if I said it was a pneumococcus, you would then ask me why, if the pneumococcus is so prevalent in normal people, that particular person is attacked? In Dr. Adler's scheme there is one thing that I cannot understand, namely, why under some circumstances there is this reaction on the part of one child, whereas many others in the same position do not show any such reaction. Of course, you will speak of the instinctive urge; and you will bring me down to the question of the hereditary factor which may or may not be present, I have never been able to convince myself positively that this factor may have such a tremendous force in the development of that person, though I cannot deny the possibility.

DR. SMITH ELY JELLIFFE: In 1910, while looking over some books in Hirschwald's Buchhandlung in Berlin I first noted "Die Minderwertigkeit der Organe," by Dr. Alfred Adler. What immediately claimed my interest was that here was a working out of an idea found in Aristotle, and which is at the basis of Lamarck's ideas on evolution, namely, that "purpose" had something to do with the working of the organism. Thanks to the freudian conceptions of the unconscious, mankind has a new way of getting at "purpose," and this is what the pamphlet dealt with. Adler, as a one-time student of psychanalysis, had employed Freud's thought and had given an interesting study. Some years later I translated the pamphlet, and gave it the title "Organ Inferiority and Its Psychic Compensation." I had hoped to hear more about this this evening.

I was much disappointed in the general pessimistic calm which settled over the situation when it was said that by the first year of infancy practically the whole story was finished. Consolidation had taken place; crystallization had been effected, and what was to be done? This reminded me of Oliver Wendell Holmes' advice that all children should take great care in the choice of their grandparents. So far as I was able to learn, Dr. Adler has told us that one ought to choose grandparents carefully in order to escape neuroses. I do not believe that crystallization is fixed at so early an age. In fact, I do not believe in the necessity for this crystallization, even when one gets to the age of Oslerization, which I am just entering. In fact, it is against all biology and all fact that if a productive, active, energetic attack on life and its forces continues, one necessarily is fixed at the age of 1, 2, 3 or 4 years, or at any other age. There is the saying, as the twig is bent the tree is inclined. It is a piece of old wisdom, but it is nevertheless not turned downward and growing into the ground; it has not entirely lost its direction toward the sun.

There are one or two things about individual psychology in which I was interested. The essayist spoke of the individual "seeking a totality," but he did not say a totality of what. He spoke of "attaining a superiority," but he did not say anything about the superiority of what. He intimated that he sought a superiority in the ego, in selfishness and in antisocial attitudes to the herd instinct (he did not call it that, but I throw it in by way of a more understandable term). I could not help thinking that he was leaving an important piece of machinery out of the picture, and that is the machinery which is much older than the ego. Weissmann has spoken of it as the continuity of the germ

plasm, and if one looks for any bit of mechanism in life, this oldest of all bits of behavior cannot be neglected in any logical concept. Dr. Adler states that "all life tends to overcome difficulties," but he did not say what the difficulties were. Are they difficulties of self-limitation, or are they difficulties of individual continuity—difficulties, therefore, of racial production? One important mechanism has been controlling evolution. What mechanism has kept life going since the stage of bacteria, or the lower algae or the lower amebas? One universal mechanism has practically remained unmodified. This Dr. Adler has neglected when he speaks of life trying to overcome difficulties, that is, those of adaptation to the sex instinct. Dr. Adler exphasizes ego behavior, but any trained biologist knows, as he surveys the innumerable botanical and animal modifications in ego behavior, spines of cacti, shapes of leaves, forms of stems, nature of tooth and claw and hoof, that all these have been developed in the interest of the sexual mechanism. The ego is important, but not so important as the race. None of this is to be found in the "individual psychology." As with the average layman, sex is repressed in this system. It does not exist.

As I heard Dr. Adler's interesting case, I could not help but feel that he had not given anything more than a behavioristic series of events. May Sinclair has given better ones. Edith Wharton has given material much superior to anything Dr. Adler has spoken of, and I think that Dr. Adler has not come to grips with his material at all. He has not said one word about the inner instinctive urge of the individual beyond this of the ego trend. The ego trend is constantly changing, whereas the continuity of the germ plasm and that which comes out of it is eternal, and has been, world without end, but not yet amen.

One thing which could be made the subject of considerable debate is the question of categories. Those who know anything about systematic zoology or botany, using those words in their generic sense, know that until a certain process was introduced into the interpretation of the different things found in plant life and in animal life, no order came into the study. In the prelinnaean days, when plants were classified according to whether they had long leaves, or thick stalks, or six petals, or five or four petals, or blue flowers, all was chaos, but when Linnaeus utilized the idea, when he studied the stamens and pistils, and got the continuity of the germ plasm idea of the marriage of the plants, then order came out of the chaos. There are still many people who believe that whales are fishes because they swim in the water. Still no zoologist believes whales are fishes. A much more important series of data concerning reproduction puts them in an entirely different category. Without the knowledge of the sexual life of the whale, no one would know it was a mammal. So I would go further and say that until the time comes when the questions suggested by Dr. Strauss can be answered along some more fundamental lines, one is not in a fair way properly to order one's house concerning disease, either from the constitutional or the dispositional standpoints. Just as the biogenetic conceptions introduced order into the natural groupings of plants and animals, I am prepared not only to suggest, but perhaps also to assert that until the same criteria can be applied to man and his diseases, until his psychosexual development can be properly estimated in the order of nature, it will not be possible properly to arrange his diseases nor know how best to combat them. Of none of these to me absolutely essential considerations, especially for the neuroses, have I heard a word tonight.

DR. ADLER: I wish to thank the three speakers for the great interest they have shown in my description; if you remember the title, I have every right to

thank you especially as you have agreed with my purpose, which is to find reasons for the occurrence and points for the prevention of the neuroses. It is not easy to remain close to the theme; the theme justifies wanderings into far countries. I am not inclined to follow all of those wanderings, but one I believe I must follow, because I have spoken of it before. The "unity of the soul" postulate in individual psychology is also influencing what is called the continuity of the species and the propagation of the species. If I do not agree with the social cult, if I deny the world, if I deny life, then this whole construction about the filaments of plants is not important. This is the difference between the soul of the human being and the plant and vegetable. This little difference gives us the hint that the propagation of mankind, sexuality, is not the most important factor in life, a constituent factor, but not the whole. It is always dependent on what I see in the world; what I foresee; what I want; and if I do not want to propagate, then this whole sexual factor is no more existent, and so really it is not vital in our culture. Persons lacking in social feeling can always be found.

Another question which I believe is more important than all others, is why one child is attacked by a neurosis and another child is not. If one is not, one person would explain it on the basis of the sexual organs, another would say inheritance; but these are not the reasons for this variation. If you do not agree with me that I can prevent the development of a neurosis, I am sure you will admit that I can make any child, in spite of his sexuality, in spite of his inheritance, become naughty; I can make every first child, in spite of his sexuality, under certain circumstances, have a neurosis, so that nobody can doubt that it is a social factor, and not an organ. It is permissible to speak of it as the herd instinct; I have called it social feeling, and I believe it is so. You can understand how this variation can exist—because there is not a wholly trustworthy method; there will be mistakes. In the education of these children also mistakes are frequent. The most important question that I would like to give you for consideration is that one can train any child to a neurosis. For instance, to be anxious, to be lacking in social relationships, to be lacking in courage—that is always the beginning of a neurosis; but I will only say one can make every child perverse if one uses the right method; therefore I think it is not possible that it is the sexual factor; the vast majority of persons are so far social that they propagate mankind. I may also say that the man who offers the sexual factor as the most important thing to be considered still must explain on what point and by what means he can prevent neuroses.

SOCIÉTÉ DE NEUROLOGIE DE PARIS

Feb. 3, 1927

Rev. neurol. **1**:207, 1927

PROFESSOR G. ROUSSY, *Presiding*

MYXEDEMA AND INFANTILE ENCEPHALOPATHY. DR. BABONNEIX.

A girl, aged 6½, presented an appearance typical of myxedema, which on further examination was found to be complicated. Dentition was retarded, the first tooth having erupted at 23 months. Language was still in the back-

ground at the time of examination. The anterior fontanel remained open after 2 years. The patient had been able to sit up only during the past two years and could hardly walk even when assisted. The height and weight were somewhat below normal. Divergent strabismus, marked defect in intelligence and rigidity of all limbs with adductor contracture were present. The size of the head was increased, particularly the posterior portions; the forehead was low and narrow; the face was moon-like, with protruded lids and thick, everted lips; the tongue was swollen and continually protruded, with exfoliative glossitis and running of saliva. The teeth were small and were separated from one another; the neck was thick and short; the thorax, compressed between the head and the abdomen, was the seat of pronounced rachitic deformity with a pronounced transverse gutter. The abdomen was large and bulging, with a small umbilical hernia. Marked constipation was present. The spine was kyphotic; the limbs were small and thin and the hands cyanosed. The expression was one of apathy and hebetude, characteristic of myxedema. The skin was yellow, rough and dry. The thyroid gland seemed to be absent. The pulse was small; respirations were short and harsh, and the temperature subnormal. There was no sweating. Walking was unsteady. She was still incontinent. The child behaved well, recognized persons and liked music.

On the other hand, the patient did not present any pseudolipoma, changes in the nails or hair, or eczema.

Three hypotheses may explain this condition: The cerebral lesions were the result of aplasia of the thyroid which was the consequence of the encephalopathy, or the thyroid aplasia and infantile encephalopathy were simultaneous and independent consequences of the same cause. The mother had typhoid fever during the fifth month of pregnancy, and it is possible that the fetus contracted the disease and had vascular lesions in the thyroid and brain.

A Peculiar Variety of Familial Spasmodic Paraplegia. Drs. Guillain, Alajouanine and Péron.

In addition to the familial spasmodic paraplegia of Strümpell-Lorrain, there are a number of other clinical varieties. A special variety of this condition is seen in two brothers presented to the society. The syndrome was characterized by: (*a*) Spasmodic paraplegia with flexion contracture of the lower limbs without marked reduction in muscular power, and the preservation of walking in a peculiar fashion; (*b*) osteo-arthritic disorders of trophic character, characterized by kyphoscoliosis resembling that of Friedreich's disease, together with deformity of the feet in talus valgus; (*c*) extrapyramidal disturbances, plastic hypertonia of the upper limb with the hand resembling parkinsonism or infantile diplegia, and facial hypertonia with fasicular twitching; (*d*) disturbances of speech and of intellectual development.

This group of symptoms permits the predication of principally cerebral lesions and the differentiation of this type of familial spasmodic paraplegia from others already described.

Cerebriform Appearance of the Skull in Certain Cases of Cerebral Tumor. Drs. Sicard, Haguenau and Mayer.

Several cases were demonstrated and roentgenograms shown dealing with intercranial hypertension and its effect on the skull. In certain cases of cerebral tumor, the skull presents ridges, thickening and atrophies which outline with

fair exactness the cerebral convolutions. This is different from the confused picture seen in Paget's disease and resembles more the finger marks that one sees in oxycephaly and hydrocephaly. It is particularly pronounced in the frontal region. It cannot be said at the present what nature of tumor would cause such an appearance, but it would seem that those located at the base produce it and that it is particularly prominent in early life and during the slow growth of the lesion. This appearance of convolutional atrophy of the skull requires ventricular hypertension to plaster the convolutions against the skull, softness of the skull and a long duration.

THE SENSORY SYNDROME OF THE PARIETAL CORTEX. DRS. GUILLAIN, GIROT and BERTRAND.

The patient, aged 73, developed left hemiparesis four years before death. The weakness receded almost entirely and left only exaggeration of reflexes and some difficulty in movement of the fingers. Jacksonian crises came on a year after the stroke, with a sensory aura in the left upper limb and movements that were limited to the left side. After the crises, the hemiparesis became more marked for a few days. Following the crises, on the left side of the body there were disorders of superficial sensation, especially in the left upper limb, along with permanent disorder in deep sensibility. The patient revealed no deformity or abnormal movements of the hands or fingers, no involuntary movements, no static or dysmetric disorder and no painful sensation to cold. There was no hemianopia, and speech and intelligence were not affected. At necropsy was found superficial softening in the territory of the branch of the left sylvian artery, affecting the lower third of the ascending parietal convolution.

INJURY TO THE RIGHT CAROTID: SYMPATHETIC PHENOMENA. DR. TRABAUD.

In August, 1925, the patient was wounded by a high explosive shell in the region of the right carotid. He did not lose consciousness and did not seem to have been severely shocked. Following removal of the foreign body, the patient noticed that the left arm was heavy and that he dragged the left foot. There was also poor control over the bladder. During the weeks following, he developed progressive weakness in the left arm, complicated by tremor.

On examination there was marked facial asymmetry, the left side being smaller and the left eye appearing smaller than the right, although there was no enophthalmos. No facial paralysis was present, although there was atrophy of the soft parts as well as of the bony parts. The left hand was somewhat succulent, cyanosed and warm. Tremor of the type found in multiple sclerosis occurred during movement. There was slight atrophy of the hand and arm, although all movements could be carried out normally and the reflexes were normal. Some hypesthesia to pain and cold was present. During the examination there were fibrillary twitchings about the left shoulder. The blood pressure on the right side was 130, systolic; 90, diastolic; on the left, 100 systolic, 90, diastolic. Sweating was more active on the right side. The patellar reflex was exaggerated, with clonus on the left but without clonus on the right. The plantar reflex was in flexion. The cremasteric reflexes were normal. A roentgenogram of the cervical region showed integrity of the skeleton and no foreign bodies. A spinal puncture revealed entirely normal spinal fluid. On electrical examination there was slight difference between the two sides.

MODIFICATION OF POSTURAL TONUS AND APPEARANCE OF BABINSKI SIGN FOLLOWING INJECTIONS OF SCOPOLAMINE IN CASES OF EXTRAPYRAMIDAL HYPERTONIA. DRS. MARINESCO and NICOLESCO.

The investigations of Marinesco and Nicolesco show that postural reflexes are generally exaggerated on the more rigid side and that postural relaxation is longer. This phenomenon is coincident with the myotonic state of the muscle brought out by percussion at its motor point.

In studying the action of scopolamine on muscular rigidity and involuntary movements, the authors observed that this substance reduced sharply the reflexes of posture, and particularly the period of postural decontraction. There is thus a functional action whose therapeutic effects have long been known but whose functional dynamic mechanism remains obscure.

Marinesco and Nicolesco were surprised some time ago by the appearance of extension of the great toe and a certain modification in the tendon reflexes a few minutes after the injection of scopolamine. The injection of scopolamine is followed by dryness of the mucous membranes and ocular disturbance, probably due to the alteration in the innervation of the intrinsic musculature of the eyeballs. These disorders reveal the selective action of the drug on these central and peripheral vegetative systems. Along with these changes, whose mechanism is still obscure, the rigid muscles become softer, the cog-wheel phenomenon diminishes in intensity, and passive movements are easier. Postural reflexes become reduced, and the duration of postural decontraction is noticeably reduced. At the same time, the tendon reflexes become more lively and the extensor response also appears, with characters that are recognized in disturbances of function of the pyramidal tract. The extension is best brought out by stroking the outer side of the foot, for scratching the inner side gives a flexion response. Sometimes this extension of the toe is found only a few times but it may remain for hours.

During a hot bath the plantar reflex is exaggerated, whatever the direction is, but there is no change in the type of response. It would seem that the hot bath brings about better conditions for the transmission of stimuli. Scopolamine, however, inverts the plantar reflex by change of conditions, probably in relation with chronaxial contractions.

In general, involuntary movements that accompany extrapyramidal hypertonia are less modified than rigidity, but they are suppressed during sleep.

Static force results from a combination of contractions of protagonists and antagonists acting on the limb segment, the result of which is to direct activities in one way. In these hypertonias, there is a contraction *en masse* that reduces the extent of movement, and under the action of scopolamine this contraction is modified and permits protagonist and antagonist to act more variably. There is thus a liberation from the "frozen" state, which permits movements impossible beforehand. Muscular power is probably not really diminished.

Injections of scopolamine have no marked effect on the grip as shown by the dynamometer. The oscillations produced by the action current are quicker following the injection of scopolamine.

These facts give certain indications of the possible association of pyramidal and extrapyramidal activities. Scopolamine exerts a sedative action on the extrapyramidal centers that arouse hypertonia. On the other hand, Rosenfeld, who has studied the action of scopolamine in other individuals, believes that its action is on the pyramidal tract because of the appearance of plantar extension. The authors believe, however, that scopolamine is, as it were, an "extrapyramidalotropic" substance; that is, that its action is essentially elective on the tonigenic centers of the nervous system. FREEMAN, Washington, D. C.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Feb. 17, 1927

DONALD GREGG, M.D., *President, in the Chair*

PARALYSIS OF THE THIRD, FOURTH AND SIXTH NERVES ASSOCIATED WITH CONTRACTED PUPIL DUE TO AN ANEURYSM, PROBABLY OF THE LEFT INTERNAL CAROTID ARTERY NEAR ITS TERMINATION. DR. DANIEL J. FENNELLY.

In 1923, several cases of intracranial aneurysms were reported by Symonds and by Cushing. Literature dealing with records of cases diagnosed as aneurysm during life is rather scanty. This case is reported both as a matter of interest and to call attention to a set of symptoms that usually means a cerebral aneurysm.

A woman, aged 43, married, who had one child about 17 years of age, last June had an attack of pain over the left eye which was followed by ptosis of the left eyelid. The condition lasted for a short period and finally dis-

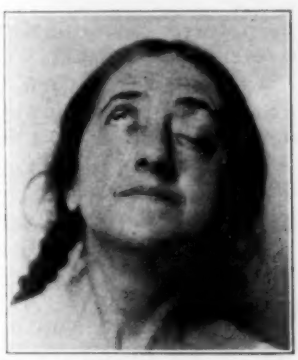

Figure 1

Figure 2

appeared without leading the patient to consult a physician. About five weeks before presentation she consulted Dr. J. A. Barre because of severe pain in the left eye and bulging of that eyeball. The Wassermann reactions with the blood and spinal fluid were negative. I do not know the number of cells in the fluid. She recently returned home from St. Anne's Hospital without a positive diagnosis having been made. She apparently had paralysis of the muscles of the left eye supplied by the oculomotor nerve; considerable bulging of the eyeball on the left side and a sluggish left pupil. The right eye was normal both as to muscles and as to pupillary reactions. There was almost complete ptosis of the left eyelid, with a disturbance in sensation corresponding to the left supra-orbital nerve. The blood pressure was 210 systolic and 140 diastolic. The heart and lungs were normal; there was a slight trace of albumin in the urine. The knee and ankle reflexes were present and equal. No sensory disturbance other than about the left eye was apparent. Dr. Cushing had her admitted to the Peter Bent Brigham Hospital for study with a possibility of operation.

Dr. Cushing's impression was as follows: "I think this is a case of cerebral aneurysm affecting the left anterior cerebral artery. Points in favor of this

diagnosis are: the suddenness of onset in each of the attacks, and the fact that there was slight clearing up of the symptoms after the first attack. The only point against the diagnosis so far as I can see is that there is no definite restriction of the visual field on the left side. An aneurysm of the left anterior cerebral artery which could involve the left third, fourth and sixth nerves and the first division of the fifth nerve should also show some signs of pressure on some fibers of the optic nerve with corresponding restriction of the visual fields. On reflection, I think it more likely that the aneurysm involves the left internal carotid artery just proximal to its termination. It is interesting to note in this case that there is a pronounced third nerve palsy associated with a contracted rather than a dilated pupil. This is probably due to a coincident palsy of the sympathetic dilator fibers which pass to the dilator pupillae in the first division of the fifth cranial nerve."

Roentgenograms, taken Nov. 13, 1926, showed a thin cranial vault without localized changes except that the channels for the middle meningeal arteries appeared deeper than usual. The pituitary fossa appeared normal, but the anterior clinoids appeared short and sharp as if due to partial destruction. There was a plaque of calcification in the falx which was apparently in the midline.

The case was demonstrated as one of cerebral aneurysm before the Harvard Medical Society. Dr. Cushing did not advise surgical treatment. Before discharge from the hospital, the patient said she thought the ptosis was less. She had remained free from attacks, with a blood pressure ranging in alternate weeks from 245 systolic and 125 diastolic to 210 systolic and 110 diastolic. She is taking potassium iodide, is resting and has been advised to avoid strenuous exercise and excitement.

An ultimately fatal outcome, with or without treatment, is assured, but life probably can be prolonged by avoiding lifting or strenuous labor and excitement.

A report from Dr. Barre, Jan. 7, 1927, showed that the patient was still living, and that the ptosis was less. The general condition was improved and the patient was mentally normal. The blood pressure was 200 systolic and 158 diastolic. On Feb. 14, 1927, the general condition was the same; the blood pressure was 190 systolic and 158 diastolic. She had had a slight attack, presumably a small hemorrhage, one week previously.

DISCUSSION

DR. H. R. VIETS: Dr. Fennelly has brought up an interesting point in regard to the paralysis of the third nerve. Although the extra-ocular muscles were paralyzed, there was no dilatation of the pupil. His explanation, paralysis of the sympathetic nerve in its course along the first branch of the trigeminal, seems reasonable. One of Dr. Cushing's early cases, in 1917, which I reported in 1918 (*J. Nerv. & Ment. Dis.* **47**:249, 1918), occurred in a person aged 26, with moderate hypertension. She had symptoms similar to those described by Dr. Fennelly, with complete ophthalmoplegia except for the sphincter of the iris. Dr. Cushing saw the aneurysm of the carotid artery at operation. The patient survived about two years; the aneurysm then ruptured, with fatal results.

DR. J. B. AYER: I saw a patient last year who answered almost exactly to this description. The patient had excruciating attacks of pain, especially in the first division of the fifth nerve. The eye subsequently became macerated. In that case a lumbar puncture made us think that we were dealing with a

localized hemorrhagic condition. We felt that we were dealing with an aneurysm. I know that the patient lived nine months, and I think she is still alive. The pupil in that case was dilated.

CLAUDE BERNARD-HORNER SYNDROME IN EPILEPTIC PATIENTS. DR. PAUL I. YAKOVLEV.

Two epileptic patients at the Monson State Hospital were mentally deteriorated. They were both left-handed and presented a curious association of a sympathetic oculopupillary syndrome and slight pyramidal signs on the opposite side.

CASE 1.—A man, aged 21, who had nothing of significance in his family history, except that the father died at 42 after a long sickness which began by shaking, progressive mental weakening, and paralysis of the lower limbs, was born at term without the use of instruments. There were no convulsions in infancy. Teething began at the average age; he began to talk at about 1 year of age, but was not able to stand or walk until he was about 4. He had always been left-handed. He went as far as the third year of high school and did ordinarily well with his studies. After leaving school he worked steadily until he had to leave on account of the attacks. The first epileptic paroxysm happened at the age of 18. At first the attacks were light, accompanied by a momentary loss of consciousness, with or without falling, but were always followed by amnesia. Later the attacks became more frequent. He began to have periods of mental confusion and psychomotor automatism; later, there were full convulsive spells with incontinence and injury. The mother had noticed that before the onset of an attack the left side of the face became flushed, the left eye bloodshot and swollen, and there was usually more or less watery discharge from the left eye. She had never noticed any flushed condition of the face, forehead or eye until after the onset of the spells. The patient had not had infantile paralysis, diphtheria or meningitis; there were no convulsions during the first ten years of life. When 16, he had measles followed by otitis media. Two years later he began to have spells. Since then the mother had noticed that he was not so bright as formerly and was becoming more childish. Memory is very poor. At the present time he is having one or two severe convulsions weekly, and nearly every day he has light attacks, blank moments with momentary mental confusion and psychomotor automatism.

Clinical Observations.—On the left side of the face there was a typical oculopupillary syndrome of Claude Bernard-Horner; the left side of the face, particularly the left cheek and left corner of the mouth, was atonic, puffy, congested and redder than the right. This side appeared a little warmer to touch; the left supra-orbital arcade seemed flattened and atrophic, and the left brow was slightly drooping; the left corner of the mouth was not so sharply outlined as the right, but the more distinct features of this syndrome were found in the left eye, the upper lid of which was puffy and slightly ptosed. The left lower lid was slightly raised, and the bow-like curvature of the edge of the eyelid was less; the conjunctiva of the left eye was congested. The eyeball was retracted (enophthalmos) and on palpation was softer and more compressible than the right. The left pupil was smaller than the right. The difference was particularly evident in darkness. Both pupils react to light and in accommodation. The eye grounds were normal except for slight hyperemia of the vessels.

I have observed several mild attacks and have been struck by the peculiarity of vasomotor display on the face preceding and following the spell. Before

the attack, all elements of the oculopupillary syndrome appear more accentuated. Vasomotor changes are more pronounced on the left side of the face, and consist of spots of vasodilatation spreading over the cheek and forehead; then the patient becomes confused, gets up and moves about the room, repeating senseless monosyllabic stereotyped sounds, as "cha-cha-cha." At the same time he beats the air with his right hand. This lasts for one or two minutes; then he "comes to himself" and does not remember what has occurred. Tests for various forms of sensibility gave negative results except that he felt cold and heat somewhat sharper on the left than on the right side of the face. Besides the left oculosympathetic syndrome, another important component of the clinical picture was involvement of the pyramidal tract on the right side of the body. Tendinous reflexes: The styloradial and ulnar on the left were less active than on the right; patellar and internal condyle reflexes also more active on the right. There was no Babinski sign but rather constant and definite combined flexion on the right side. At the same time, subjectively, he complained of cramps in the right leg; in walking there was slight dragging of this leg. To this may be added that in the heel-knee tests he showed a peculiar incoordination on the right side which suggested both cerebellar asynergy and pyramidal spasticity. The Wassermann reaction was negative and the spinal fluid normal.

Case 2.—A girl, aged 19, whose family history is negative with regard to syphilis, tuberculosis, insanity, or nervous disease, is the second of three children; the mother also had two miscarriages after the patient was born. There was nothing abnormal at birth, and motor and mental faculties developed normally. At the age of 14 months she fell from a table, and following this had a series of convulsions. After the fall she was paralyzed on the right side of the body, but three weeks later the paralysis seemed to recover. She had convulsions until the age of 5, usually petit mal attacks of irregular frequency. The attacks then ceased. Menstruation was established at 12, and at 15 the spells reappeared. She had them usually in a series of three or four in one day, and for two or three days; then she might go for a few weeks without any. The attacks started in the right hand which began to twitch; they were mild and without generalized convulsions.

Neurologic Examination.—This patient also had an oculopupillary syndrome on the left side, not so obvious and constant as in the former case, but distinct. There was a narrowing of the left palpebral fissure, enophthalmos and diminution of ocular tonus; at times flushing of the left side of the face, inconstant but distinct myosis of the left pupil and heterochromia of the irises, the left eye gray, the right brown. Indubitable signs of a pyramidal lesion existed on the right, similar to those described in case 1. This patient was left-handed. Segmental force was diminished in the right arm and leg, which were relatively hypotonic. The patellar and achilles reflexes were more active on the right side. No Babinski sign was evident, but there was a distinct combined flexion on the right side. Moreover, there was slight incoordination in the finger-nose test on the right side, with intention tremor and slowness of alternative movement in the right hand; these apparently cerebellar features in the presence of pyramidal signs on the same side are difficult to interpret.

Comment.—The interesting feature in these two cases is the association of a sympathetic oculopupillary syndrome, presumably of central origin, with epileptic paroxysms, left-handedness and pyramidal deficiency on the opposite side. In case 1, in which epilepsy began in later life, the sympathetic syndrome apparently developed about the same time. There was no hetero-

chromia. In case 2 epilepsy first appeared in early childhood, and the sympathetic syndrome was apparently of congenital type since there was distinct heterochromia of the irises. Association of epilepsy and oculopupillary syndrome is not unusual. Among about 350 cases examined within the last year, I have found three with an oculopupillary syndrome, by curious coincidence always on the left side. In these three cases also, there were objective signs of organic lesion in the central nervous system. In one there was a bilateral Babinski sign; in another asymmetry of tendinous reflexes and combined flexion sign; the third was a rare case of postencephalitic epilepsy with an extrapyramidal syndrome of the parkinsonian type. The fact of the association of epilepsy with central, organic signs and with a sympathetic syndrome suggests that this last was also of central, not peripheral, origin. It is probable that an organic or functional trouble of the cephalic part of the sympathetic system may be at least a secondary or intermediary factor in the production of epileptic paroxysms.

DISCUSSION

DR. STANLEY COBB: Is there any atrophy of the face?

DR. YAKOVLEV: Yes, he has some atrophy of the left supra-orbital arch.

DR. D. J. MACPHERSON: Is there any local sweating on that side of the face?

DR. YAKOVLEV: No. I could find no excess of sweating but the difference in coloration is sometimes pronounced. The hair is drier on the left side of the head.

DR. DONALD GREGG: Does the hair grow faster on one side than on the other?

DR. YAKOVLEV: No. It is about the same, except that the hair is not so elastic as on the right side; it is dry and somewhat more erected.

DR. COBB: I am especially interested in these cases because for the last year Dr. Forbes has been experimenting in my laboratory, stimulating sympathetic nerves and observing the pial arterioles within the skull through a window and microscope. I think he has evidence that there is, after stimulation of the cervical sympathetic nerve, a distinct contraction of the arterioles within the skull. For a long time we have had a clinical explanation of many syndromes on the basis of vascular spasm. Now, perhaps, we have evidence along that line in Dr. Yakovlev's patient. However, there must be a decrease of function in his cervical sympathetic nerve, because he has a Horner's syndrome, and with loss of function of the sympathetic one would expect within the skull a vascular dilatation if there is anything in our experiments. Is there any relationship between the Horner syndrome and the convulsive movements on the opposite side? One might think of operative interference to correct this instability of the left sympathetic by sympathectomy on that side. If one operated in this way, would one stop the fits or make them worse? In cervical sympathectomy on animals one almost always has enophthalmos, myosis and vascular dilatation on that side. It is especially obvious in the ear, which is warm and red afterward. This patient has a spasmodic defect, and perhaps operation would relieve him by stopping the variability of reaction, but it is all more or less speculative.

DR. H. B EATON: Is not the work Dr. Cobb described as being done, especially on rabbits, direct evidence of the connection between vasomotor reaction and spells or fits? It seems to me that pathologists once again are bearing out, by experimental work, the theory of vasomotor instability which has long been held clinically.

Dr. H. R. Viets: The unusual thing about one of the cases is the late development of the Horner syndrome. This syndrome is often found in epilepsy. Oppenheim speaks of a paper by Negro, who examined a large number of patients. He felt that the Horner syndrome was a common stigma of degeneracy, especially in cases of epilepsy.

Dr. M. B. Hodskins: Twenty-five or thirty years ago we used to see a great many patients on whom cervical sympathetomy had been performed, but I never saw one in whom the operation had the slightest effect on the epileptic attacks.

Dr. Yakovlev: There is no true and definite paralysis of the cervical sympathetic as we see in those quasi-experimental traumatic cases with transection of first, second and third dorsal roots. It is more a kind of temporary sympathetic deficiency which makes the syndrome more pronounced one day and less pronounced another day. This is rather a characteristic feature of the semiology of the nervous system in epilepsy. There are two types of clinical signs associated with epilepsy: permanent, constant signs of an organic lesion, as, for example, infantile hemiplegia; inconstant signs, for example a definite Babinski sign for a few hours only, indicative of a temporary functional disturbance rather than of a structural lesion. There is a feature which, I believe, speaks against a congenital type of syndrome in case 1, namely, absence of heterochromia of the irises which is typical of the congenital syndrome of Bernard-Horner. This patient had measles complicated by otitis media at 16, thus giving a valid etiologic condition for the sympathetic trouble. Relatives of the patient say that they have noticed the flushed condition of the left side of the face and swelling of the left eye only after or at the time when he began to have epileptic attacks. I believe that in some cases a congenital or acquired disorder of the cephalic part of the sympathetic system might be considered as an intermediary or secondary factor in the mechanism of epileptic paroxysms.

Brief Outline of a Personal Theory Concerning the Pathogenesis of So-Called Posterolateral Sclerosis. Dr. J. W. Courtney.

For a considerable number of years I have been collecting data bearing on the identity, from a pathologic standpoint, of those clinical syndromes to which the inapt descriptive terms hysteria, psychasthenia, migraine, epilepsy and acute psychosis cling with limpet-like tenacity. On the phylogenetic side the results of my research have been interesting and illuminating. For example, a migrainous or epileptic parent may transmit to the offspring the affliction as such. The same is true of the psychotic or the hysterical disorder, but often the parental disorder is metamorphosed in transmission. Not infrequently migrainous parents breed children who are asthmatic, epileptic or hysterical. The heterogeneity of the morbid transmission is striking and suggestive.

The transformations the various syndromes under consideration have undergone clinically also are striking and suggestive. In numerous cases, a patient who has for years suffered from typical epileptic seizures, ceases to experience them and has, in their stead, periodic headaches which conform in every particular with migraine. The converse of this situation is likewise an established fact. Time and again I have seen patients have now a migrainous headache, now an attack of either grand or petit mal. I have notes of a case in which a typical migraine of twenty-four hours' duration was habitually the aura of an attack of grand mal. Finally, we all know that psychotic episodes, varying in character from depression to violent mania, may serve

as equivalents of either a migrainous headache or an epileptic seizure. I cannot refrain from adding that, were we entirely candid, we would admit that we have not a single infallible criterion which we may apply to the phenomena of a given seizure, and thereby determine that this seizure is epileptic or hysterical. Certain authors would impose amnesia as this criterion, but in the crises of so-called intellectual petit mal, contact with reality is not always entirely severed; in consequence, certain episodes of the attack register in consciousness and for them memory survives. On the other hand, in the somnambulisms, induced or not, of the hysterical patient, many things are experienced for which, in the waking state, memory is blank.

In view of all these facts, I venture to draw the following conclusions: 1. The clinical syndromes which bear such purely descriptive labels as epilepsy, migraine and hysteria — labels, furthermore, which came into use many centuries before the birth of scientific pathology — together with those bearing labels of later date, to wit, psychosis and psychasthenia, do not, in the last analysis, constitute clinical entities but represent merely so many quantitative variations in site and activity of one and the same pathologic process. 2. By reason of the early age at which the morbid phenomena embraced in the syndromes in question may appear we are warranted in concluding that the morbid agent productive of these syndromes is inherent in those embryonal elements from which develop the blood vessels and the autonomic nervous system.

So far as I know, the accepted view is that the phenomena of the syndromes under consideration are due to abruptly or relatively abruptly occurring variations in circulation. There are, for example, migrainous headaches due to vasoconstriction or to vasodilatation indifferently. To what extremes these fluctuations may attain we may judge by the fact that after certain attacks of so-called ophthalmoplegic migraine fresh hemorrhages are observed in the retina. And in the case reported by Dr. Fennelly, a case in which the clinical phenomena coincide absolutely with those described both by Oppenheim and by Flatau as pathognomonic of ophthalmoplegic migraine, I cannot bring myself to look on the aneurysm, which is now undoubtedly present, in any light except that of an end-result of severe and many times repeated vasomotor storms in the region involved. I do not know the intimate nature, pathologically, of the process which gives rise to these storms; hence, I am constrained to apply to it the designation, descriptive, furthermore, congenital vasomotor ataxia.

To come now to my theory: I think that, in the disorders termed migraine, epilepsy and hysteria, for example, observers are prone to focus attention on such outstanding symptoms as headache or convulsive seizures and to neglect the large group of concomitant or equivalent phenomena which, in a given case, springs from a pathogenic mechanism identical in kind with that which produces the symptoms to which I have just alluded. In a migrainous case, for instance, we may have, in addition to the headache, which may be of any conceivable degree of severity, such symptoms as cranial nerve palsy, hemiplegia, hemianopia, hemianesthesia, motor or sensory aphasia — the list is a long one. Even anginal attacks are not of great rarity; and it is well known that in young migrainous subjects abdominal phenomena may occur which so closely resemble appendicitis as to lead to surgical intervention.

A number of years ago I saw, rather close together in point of time, several cases presenting the clinical picture of combined sclerosis of the posterior and lateral tracts of the cord. One or two of these patients also had migraine,

and all had a migrainous ancestry. Since that time I have carefully investigated every case of so-called combined sclerosis and have been struck by the regularity with which I have found an associated migraine in the patient or a history of migraine in the family. I have long since been convinced that the association is not merely a coincidence. If we study closely the clinical history of combined sclerosis, we find that its progress is not steady but intermittent; if we study its pathologic processes we find that it has none of the attributes of an inflammatory process. I venture then to regard so-called posterolateral (combined) sclerosis not as a clinical entity, but merely as an end-result (analogous to the permanent phenomena observed in migraine) of that congenital vasomotor ataxia to which we may, I hold, ascribe the syndromes now improperly designated, respectively, hysteria, epilepsy, psychosis, psychasthenia and migraine.

DISCUSSION

Dr. J. B. Ayer: It is difficult for me to see how a vasomotor disturbance can produce a fixed lesion, such as posterolateral sclerosis. Practically all the phenomena we associate with vasomotor disturbance are conditions that we believe to be physiologic, for example, epilepsy and migraine. However, one has presumably an example to the contrary in Raynaud's disease, but in this disease one is dealing with terminal vessels, whereas in the spinal cord there is a rich anastomosis, and in the case of the spinal cord it seems unlikely that it would be possible to cause a prolonged blanching sufficient to lead to a fixed pathologic lesion. It is of interest that Dr. Courtney has found evidence of migraine, associated with posterolateral sclerosis, but that the relationship is necessarily on a vasomotor basis is not apparent.

Dr. H. R. Viets: It might be pointed out that the pathologic process of posterolateral sclerosis covers a larger area than the posterolateral columns. It is really a diffuse process of the whole spinal cord.

Dr. Courtney: I consider that this theory concerning the pathogenesis of so-called posterolateral sclerosis has been stated clearly, and that it is worthy of consideration only so far as it approaches the truth. I regard it merely as an effort to simplify our conception of the pathogenesis of a group of pseudo-entities in the realm of so-called functional disorder of the nervous system. I am willing to let time pass on the tenability of my views.

1. A Case of Myelitis of Unusual Etiology.
2. Dislocation of Lower Lumbar Vertebrae, with Consequent Hemorrhagic Myelitis in the Cauda Equina.
3. Bullet Wound of Frontal Lobe. Dr. J. W. Courtney.

Case 1.—This patient was a man whom I showed before this society at the meeting of Oct. 18, 1923. (A case of Myelitis of Unusual Etiology, Arch. of Neurol. & Psychiat. **11**:223 [Feb.] 1924). The patient was then 47, and had been referred to me by Dr. MacAusland. His health had been excellent until October, 1922, when he had an exceptionally severe attack of bleeding piles. For two months the loss of blood at stool was profuse. At the end of that time he noticed numbness of the right great toe followed by a burning sensation in the ankle. This was followed by marked trepidation in the muscles of the right lower extremity. The numbness gradually extended from ankle to knee and from knee to the lower abdomen. About three months later, numb-

ness and trepidation appeared in the left lower extremity. The numbness ultimately reached a level just above the symphysis. At that time great difficulty was experienced in starting the urinary stream, although the urine was passed freely with the stools and the patient could feel the flow. Defecation was difficult, but there was no loss of sensibility in the rectum. There has been no pain aside from a "neuralgic feeling" in the knees. For eight weeks prior to my first examination there was dragging of the right leg, and for three weeks the left leg had been spastic. There was no disturbance in the power of erection; the upper extremities were not affected. The numbness experienced up to the time the left leg became spastic was purely subjective. Physical examination at that time showed a fairly well nourished but rather pallid man. Walking or even standing without assistance was impossible. The gait was not only spastic and ataxic, but it was further embarrassed by an extraordinarily severe myoclonus which involved practically all the muscles of the leg. The heart area and sounds were normal. The spine was normal in contour and flexibility. With the patient seated, the clonic spasms diminished markedly, but voluntary movement increased them at once. Muscular atrophy was entirely absent. All forms of sensibility were blunted but not lost throughout the legs to the level of the symphysis. The knee and ankle jerks were enormously exaggerated. The slightest upward pressure on the plantar surface of the foot produced a violent and persistent ankle clonus. The Babinski phenomenon could almost be produced through the sole of the shoe. Weakness of the lower extremities was marked.

Comment.—In arriving at an etiologic solution of the case I could not escape the conviction that the appearance of the primary numbness of the right great toe synchronously with the severe hemorrhoidal attack was not a mere coincidence. The free anastomosis of the hemorrhoidal system with the spinal system suggested strongly that one of two things had taken place: either an upward extension of hemorrhoidal thrombi or an infection through these veins. The case was referred back to Dr. MacAusland with recommendation that an immediate exploration of the rectum be made. This was done by Dr. Ralph Jackson who found a definite internal hemorrhoidal condition, more marked on the left side of the anus, and an indurated column running upward toward the seminal vesicle on the right side of the ampulla. The latter was not tender or discernibly fluctuant; it felt like scar tissue, and was suggestive of a sinus, though he could find no opening. Dr. Jackson made a radical hemorrhoidal incision. Before the patient left the hospital the trepidation of the legs had ceased. When he next came to my office he had no support other than an umbrella. At a later time he came alone and without any artificial aid to locomotion. He has been at work for nearly three years now. His gait is brisk and shows no peculiarity. The reflexes are lively on both sides and there is a suggestion of clonus on both sides but, in view of what the patient presented in this respect three years ago, I should call the present status of the reflexes practically normal.

Case 2.—The patient was a married woman, aged 31, an operator in the action room of a piano factory in Cambridge whom I saw at the Cambridge Municipal Hospital, Oct. 13, 1926. The story elicited was: Some time in the second week in August, while the patient was working, the foreman came to speak to her and spat a mouthful of tobacco juice on the floor. The patient was cleaning around the machine. She started to pick up a little barrel in which she kept waste; the right leg slipped on the tobacco spit and shot forward, while the left went backward. The head went backward and hit

the floor. She experienced an immediate stabbing pain in the spine just above the sacrum and extending somewhat upward. She had a further stabbing pain under the right scapula. She lay in this bizarre position for about five minutes. She is unable to say whether or not she lost consciousness to any degree. Finally, she got a grip on the machine and pulled herself up. She made her way to the next bench and ate lunch. She was still in pain. She continued to work in the afternoon but had to sit down to it. She has not been able to work since. The symptoms following the accident, other than pain, were: weakness in both lower extremities, particularly the left; paresthesia of the legs, particularly the left, extending from the toes to a point well above the knees, and vesical incontinence. The patient was ultimately taken to the Cambridge Municipal Hospital and put on a Bradford frame. When I saw her some weeks later she was sitting up in a chair but unable to walk without assistance. The gait was spastic-ataxic to a certain extent and a Romberg sign was marked. The cranial nerves and upper extremities were not involved. There was no atrophy of any muscles in the lower extremities, but there was considerable weakness, particularly of the left. The knee and ankle jerks were both lively and the Babinski sign was present on both sides, particularly marked on the left. There was some clonus on that side. Extending from the toes up, and particularly on the posterior surface of the legs, there was a band of anesthesia extending to a point about 3 inches (7.6 cm.) above the bend of the knees. On the left side this area was also analgesic. A roentgenogram taken prior to this time showed no evidence of fracture or dislocation of vertebrae. My diagnosis was "dislocation of the lower lumbar vertebra with consequent hemorrhagic myelitis in the cauda equina;" I advised putting the patient in a plaster cast and in bed. She gradually regained power in the legs, and the sensory disturbances disappeared from the right leg. She was discharged from the hospital on Jan. 10, 1927. At that time she still complained of pain in the spine and of urinary incontinence. I recently saw her in her home. She continues to have pain in the back and says that she has not regained proper control of the bladder. The gait is not strictly spastic or ataxic, although she gets about only with difficulty. She ascribes this difficulty to the persistence of the pain. The knee and ankle jerks are lively on both sides, but there is no clonus. There is, however, a Babinski sign on both sides, rather more marked on the left. The sensation of the right lower extremity is practically normal. On the left there is hypesthesia and hypalgesia in the area already referred to. There is no atrophy and the gross strength of the legs is fair, but there is a certain muscular trepidation to be observed in the left thigh group, even when the patient is lying quietly on the back.

Case 3.—A widower, aged 75, whose family and previous histories are unimportant, on Nov. 15, 1926, was brought by the police to the Cambridge Municipal Hospital with the story that he had become despondent over the loss of a position, which he had held for twenty-seven years, and had determined to end his life. With a twenty-two caliber revolver he fired a shot almost at contact into the right frontal region of the skull. Nothing, apparently, resulted, not even a slight loss of consciousness. The patient fired a second shot, also practically at contact, close by the first. About this time the police interfered and the man was brought to the hospital. When first seen in the accident room he was conscious and rational; his only complaint was dizziness. There were no marks from powder around the points of entrance of the bullets. The pupils were equal and regular and reacted to light and distance.

There was no paralysis of any degree anywhere. The knee and ankle jerks were present and equal. There was no Babinski, Gordon or Oppenheim sign and no clonus. On the day of admission a roentgenogram showed two large pieces of metal slug with several smaller fragments in the right frontal region and a bullet hole where a large slug entered the skull. The following day the patient was still conscious, rational and rested comfortably. All reflexes were normal. There was complaint of slight headache on the right side and occasional dizziness. The temperature was 98 F., the pulse rate 64 and respiration rate 24. When I saw him on Dec. 1, 1926, he still complained of occasional dizziness but was sitting in a chair. Complete physical examination gave entirely negative results. The patient was discharged on Dec. 9, 1926, still complaining of occasional slight headache and dizziness. During his entire stay in the hospital the temperature never reached 100 F., but the pulse rate was for the most part about 80 and on several occasions reached 90 or a little over. The respiration rate was invariably 24.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Feb. 17, 1927

JOHN FAVILL, M.D., *President, in the Chair*

INCIDENCE OF HEADACHE AND FAINTING IN ADULTS: ITS RELATION TO CONVULSIONS, HEAD-BANGING AND BREATH-HOLDING IN THEIR CHILDREN. DR. DAVID M. LEVY and DR. HUGH T. PATRICK.

This article will be published in full in a later issue.

THE PATHOGENESIS OF CEREBRAL HEMORRHAGE: A CASE OF ANEURYSM OF THE POSTERIOR COMMUNICATING ARTERY. DR. G. B. HASSIN.

This paper will be published in full in a later issue.

TUMOR OF THE CAROTID BODY. DR. EUGENE F. TRAUT.

This paper will be published in full in a later issue.

INCIDENCE AND TEST PERFORMANCES OF "KRETSCHMER TYPES" AMONG CONVICTS. DR. GEORGE J. MOHR.

The physical types as defined by Kretschmer, the asthenic, athletic and pyknotic builds, resemble similar classifications made by numerous previous investigators. Among convicts these forms can be found readily, but they cannot be sharply differentiated by inspection or by physical measurements. A crude index of build places them in the following order: asthenic, athletic and pyknotic, that is, the athletic build is intermediate in almost all physical measurements and proportions. The incidence of "pure" types among 254 convicts—"pure" asthenic 17.8, "pure" athletic 36.6 and "pure" pyknotic 9.8 per cent, with many intermediate forms—indicates a normal distribution of the "types" with asthenic build at one end, athletic forms at the mean and pyknotic types at the other extreme of the normal distribution curve.

The "best" asthenic, athletic and pyknotic forms among 600 convicts were selected, and of these ninety were tested by various criteria. (Mohr, George J.,

and Gundlach, Ralph H.: The Relation of Physique to Performance, to appear shortly in the *Journal of Experimental Psychology*.) The army alpha scores indicate that the asthenic men are brighter, the athletic intermediate and the pyknotic the dullest. An information test of the multiple choice type bears this out. The asthenic men are younger than the athletic, and the pyknotic men are the oldest. The performance on intelligence tests is, however, independent of age. In reaction time and speed tests the order is the same as that indicated by the army alpha scores. In tests of attention (Young's light series and Franz dot-tapping test) the asthenic men lose their foremost position and the athletic men do better. In learning tests the pyknotic men do relatively better.

Social data show that while there is a marked preponderance of crimes against property committed by all three groups, the proportion of crimes against the person, such as assault and sex offenses, is much greater among the pyknotic men. Although they are older, the pyknotic men have previous prison records much less frequently. Pyknotic men marry more frequently, and tend to join fraternal organizations, but age is a factor to be evaluated in this connection.

The conclusion is reached that differences in performance can be demonstrated among the groups differentiated on the basis of physique. These differences are statistically significant. They tend to prove that the asthenic subjects show relatively more schizothymic tendencies, since in tests involving attention and learning the asthenic subjects do not do so well as those in the other groups. Disorders of attention and association are presumably characteristic of schizophrenia. The pyknotic subjects show more cyclothymic tendencies according to both test performances and social data. In general, the results indicate that while there is a relation between physique and character of performance as proposed by Kretschmer and others, there is no evidence of the existence of clear-cut types or of focal points or "nuclei" (Kretschmer) around which are grouped the types of personality. The results indicate a continuous progression of performance linked with a similar progression of physical characteristics passing from those that define the asthenic through the athletic to those that characterize the pyknotic subjects.

DISCUSSION

DR. HERMAN M. ADLER: This subject has particular bearing on certain aspects of psychiatry. Dr. Mohr's paper has suggested certain ideas to me. There seem to be two categories with which we are dealing, and it is important to differentiate between them. The first includes qualities that are common to all human beings and in which the question is merely one of how much or how little; in other words, this is, as the logicians say, the category of "more or less." Contrasted with this are qualities that come under the category of "all or nothing," that is, a person either has or has not this quality. Intelligence for instance, belongs in the former category; disease in the latter. Kretschmer has attempted to correlate certain types of personality with physical constitution on the "all or nothing" basis. According to the observations of Dr. Mohr, these same criteria indicate that personality should probably rather be classified under the "more or less" concept. If the group studied is large enough, it seems that these qualities group themselves according to the law of distribution. Dr. Mohr's graphs show such curves of distribution and indicate, therefore, that the items charted are common qualities and follow the logic of "more or less."

It may be proper to raise the question, therefore, whether some of the psychiatric classifications should not also be transferred from the "all or nothing" category to the "more or less." For instance, that bugbear of the older writers, paranoia, has never been justified as an "all or nothing" phenomenon. It may be that the difficulty will be removed if paranoia will be regarded as an extreme manifestation of a "more or less" variation. If this should prove tenable, it should be possible to find persons at the other end of the scale who are extreme variants in the direction of generosity, unselfishness, and subordination. Further work will undoubtedly give further evidence on this point which should help in differentiating in respect to the two categories.

When this logic is applied to groups, the difficulty increases, for after a person is placed in a low grade, for instance, because of objective observations, it is not always possible to differentiate between biologic variation and accidental factors applying to that person alone. Thus in any given case it is impossible, at least at one examination, to determine whether a particular person is low grade intellectually because of racial or innate qualities, or whether his low mental stature is the result of acquired or pathologic interferences. Theoretically, we can assume that there are two kinds of stupidity at least, the acquired pathologic one and a normal and healthy stupidity. In setting up programs to deal with low intelligence, it is obvious that this distinction is of great importance. I may add that the object of scientific inquiry, among other things, is to remove as many persons as possible from the "more or less" category, and transfer them to the "all or nothing" category. As our knowledge of precise relations in any particular pathologic condition increases, we should be able in increasing extent, to place them in the "all or nothing" category.

Dr. Charles F. Read: Has there been any attempt to check up on the reactions to prison life in the different types? If so, was the behavior significant of what might be suspected of the type?

Dr. Clarence A. Neymann: I have heard this discussion of the pyknotic and asthenic types not only here but also at other neurologic society meetings. Is it not a general fact that when confronted by a phenomenon of nature, man makes an artificial classification? The patient is then classified; later the classification is found inadequate, and then finally we say "the types merge." There would seem to be no definite measurement for these types.

I was much impressed at another society meeting by the presentation of an old, fat and short manic patient, and of a young, athletic, tall, schizophrenic patient. These persons were selected as good examples. The question arose as to how much was real and how much was volitional, and if one had the opposite conviction could one not have selected a fat, old schizophrenic, and a young, tall manic patient?

In the tests that were used, was any attention paid to the stage that the pyknotic person was in? If the patient happened to be in the depressed stage, his reactions would, of necessity, be slowed down, and he would be shown to be rather stupid when measured by intelligence tests; if he was in the manic stage, he might be shown to be bright.

I leave it to further investigation to ascertain whether these really exist. We must have two definite factors: definite physical measurements and definite psychologic measurements. In this way presumptive personal elements that now cloud the issue will be eliminated.

Dr. Mohr: As to the matter of applying artificial distinctions and breaking them down, this certainly occurs, but it constitutes a valid attempt

to arrive at further understanding of the psychoses. Kretschmer did an artificial thing, but his views are helpful and are, in part at least, based on demonstrable fact. The relationship of the manic-depressive psychosis and pyknotic build apparently holds. Our present observations do not break down but carry along the same idea, showing, however, that the relationship between physique and "temperament" dealt with by Kretschmer does not necessarily imply acceptance of a concept of "types" of physique.

As to how much is real and how much is not real with respect to determination of the physical forms described, we are agreed that it is not possible to differentiate types. Anthropometric technic is being developed, however, which will probably soon remove most subjective elements in description of physical forms. Subjective elements can probably not be entirely eradicated.

As to the mood that the men of presumably cyclothymic temperaments were in, we were not dealing with manic-depressive patients, but with men who were normal, except that they were convicts. None of them betrayed either excitement or depression, and presumably any variations present would lie within the limits considered normal.

Book Reviews

LES DYSTONIES D'ATTITUDES. By ANDRÉ THEVENARD. Price, 28 francs. Pp. 191. Paris: Gaston Doin et Cie, 1926.

In this monograph the author undertakes the large task of correlating clinical observations, physiologic facts and speculative deductions in the study of dystonia, both as a symptom and as a clinical entity. He has evidently read a great deal, collected many case reports, gathered a number of experimental facts, made a few clinical observations and indulged in considerable speculation. The result is a stimulating but uneven monograph, and the conclusions arrived at are not quite warranted by the facts presented. They would be interesting, if true.

The author begins by considering the muscular actions that govern normal standing and stresses their tonic influence in its maintenance. He would divide the body musculature into groups belonging to anterior and posterior planes, the latter dominating in the maintenance of standing posture. He passes lightly over the physiologic grouping of flexors and extensors and departs considerably from the sherringtonian conception of the action of the antigravity muscles, without adducing new experimental facts. Next he describes the forward and backward thrust phenomenon (le phénomène de la poussée) to illustrate the action of the anterior and posterior groups of muscles in maintaining normal equilibrium. This consists of the prevention of falling by the contraction of the whole anterior group of muscles if a person who is standing is suddenly pushed backward, and of the posterior group if he is pushed forward.

In the third chapter is discussed the physiologic character of muscular action and normal equilibrium in relation to postural tonus, which the author would rather designate as tonus of attitude. In the next he reviews postural synergies, as revealed by pathologic studies, and takes up the tonic neck and labyrinthine reflexes of Magnus and de Kleijn. The fifth chapter contains a summary, from the literature, of cases of dystonia musculorum deformans or torsion spasm. These he calls "the grand pathologic disturbance of the tonus of atittude." Evidently the author is not personally familiar with the manifestations of dystonia as an independent clinical entity, but has observed a number of patients with symptoms of dystonia who previously had encephalitis. He makes the positive assertion that the dystonia in torsion spasm disappears on lying down —a statement easily contradicted by simple observation. Apparently the author overlooks the fact that much water has flowed under the bridge since Oppenheim and Ziehen first described those cases.

In the sixth chapter, torsion spasm is considered in relation to decerebrate rigidity, but here again the author speaks of cases caused by encephalitis. He interprets the dystonia as waves of decerebrate rigidity and the postures as fragmentary manifestations thereof. Apparently he is not aware that Wechsler and Brock (*Arch. Neurol. & Psychiat.* **8**:538 [Nov.] 1922) have called attention to the presence of signs of fragmentary decerebrate rigidity in dystonia and have also spoken of myostatic and myokinetic forms of that disease. Although previously emphasizing them, he now ignores the actions of the neck and labyrinthine reflexes on tonus.

The seventh chapter deals with the relation of torsion spasm to athetosis, Wilson's disease and pseudosclerosis, all in the light of dystonias of attitude;

that is, postural dystonia. He objects to the correlation of dystonia with Wilson's disease, as Hall has done in the discussion of hepatolenticular degeneration, and insists, correctly in the opinion of the reviewer, that dystonia is a symptom which must be studied in different pathologic conditions and accounted for by involvement of certain groups of cells or pathways. In the next chapter, torticollis is considered as a localized dystonia (of attitude), the spasmodic form in relation to dystonia proper and the clonic variety as related to athetosis. The ninth chapter contains a brief exposé of the mechanisms of posture and a review of the anatomic and physiologic studies in experimental decerebration, the tonic neck and labyrinthine reflexes, and the postural disturbances in experimental lesions of the cerebellum. Finally, after detailing a number of case reports, the author restates the conclusions arrived at in the preceding chapters.

It is difficult to criticize a monograph of this character. It deals with a subject that is far too complex for the clinician and presumes to discuss a number of problems, each of which demands extensive experimental physiologic investigation, detailed anatomicopathologic studies and numerous meticulous clinical observations. While the attempt to correlate well known facts is often justified and even necessary, the author does not present any new facts and contributes little to the present knowledge. The monograph represents too facile an attempt to crystallize views that are still obscure and to simplify a subject that is all the more complex because of the many gaps in the knowledge of anatomy and physiology. Such a study, stimulating though it is, illustrates the danger of armphysiologic experiment—a pastime in which, unfortunately, some neurologists chair speculation in a field that must be based on anatomic observation and delight in indulging.

GOITER AND OTHER DISEASES OF THE THYROID GLAND. By ARNOLD S. JACKSON. Price, $10.00. Pp. 353. New York: Paul B. Hoeber, Inc., 1926.

There is always something to be said in commendation of a book that deals solely with some particular organ or structure. For completeness, however, such a book must consider the relationship of that organ to the other structures of the body. Not to do so limits its usefulness, and Dr. Jackson's book leaves something to be desired in this respect. The best chapters are those which concern themselves with exophthalmic goiter, adenoma of the thyroid, and the uses of iodine. It is evident that the author considers the subject from the standpoint of the surgeon, which takes the book out of the class of monographs. Consideration is given to the points of view of so-called "goiter specialists," and the author justly criticizes some of the pernicious doctrines. Bram's dictum that surgery is indicated in exophthalmic goiter only when there are signs of pressure or a malignant condition is an absurdity, in the author's estimation. He states that "Pressure symptoms and malignancy are never observed in exophthalmic goiter."

Unfamiliarity with the various types of apparatus used in determining the basal metabolic rate and lack of experience with the Kottman serum test are frankly admitted. A surgeon specializing in diseases of the thyroid should at least be sufficiently interested in these various tests to inform the reader of their merits or demerits. The busy practitioner wants to know these things. The author mentions the Goetsch and Kottman serum tests merely to state that he does not approve of them: "A much simpler test for hyperthyroidism is to place the patient on small doses of iodine; a marked clinical improvement points to a *possible* exophthalmic goiter" (the italics are by the reviewer and not in the original). Considerable space is devoted to iodine

hyperthyroidism and crises of hyperthyroidism, which are well handled. When he deals with the subject of hyperthyroidism after removal of the gland, the author is not clear and evidently does not know what the condition is. It is rather a "reductio ad absurdum" to state that the symptoms of overactivity of the thyroid can occur after the removal of the gland. Iodine metabolism may be the factor here, but it is not considered. And by the same token, why does not some author consider the problem of iodine metabolism after thyroidectomy? This, of course, would be expecting too much of the surgeon, whose chief interest in disease of the thyroid is operative results and lowered mortality statistics, and who does not expect to treat the patient after the stitches have been removed. The term "physiological goiter" is mentioned, but not clarified. A scientific treatise on diseases of the thyroid gland should certainly classify this condition and not leave the reader "up in the air."

The text is generously illustrated (151 illustrations in all); but what deductions can be drawn from photographs in cases of exophthalmic goiter showing the patient looking upward before operation, thus enhancing the width of the palpebral fissures and looking downward after operation, thus lessening it? The reader must take the author's word for it, apparently.

The author's differentiation of hyperthyroidism from nervous disorders merely scratches the surface and shows an unfamiliarity with nervous diseases. His is again the point of view of the surgeon—every nervous disorder is merely "nervousness." He states: "Neurotic young women who are underweight, who complain of a rapid heart, palpitation, tremor and so forth, and who present a symmetrical enlargement of the thyroid and bruits, often furnish a difficult problem in diagnosis. The establishment of a normal basal metabolic rate in these cases at once eliminates the possibility of hyperthyroidism *and surgery*" (italics by the reviewer). In another chapter, the metabolic rate is considered totally unreliable, and all the emphasis is placed on the clinical observations or iodine therapy. What, then, is a neurotic young woman? and what is hyperthyroidism? So long as it is not a surgical case, it does not matter. Focal infection and its rôle in disturbance of thyroid activity is dismissed with a few brief statements.

The book on the whole is well written and is easy reading, except for the glossy paper. A large bibliography is appended, and shows that all of the author's papers on this subject, except one, have been published since 1923. The subject matter is concisely handled. The too frequent use of the pronoun in the first person singular detracts from, rather than adds to, the book. The book will be mainly of interest to the surgeon, for there are more extensive works on the anatomy, physiology, pathology and symptomatology of the thyroid, together with a wider interpretation of its influence on the organism.

GRUNDRISS DER KRIMINALBIOLOGIE. By DR. ADOLF LENZ. Pp. 252. Price, R. M. 15; geb. 16.80. Vienna: Julius Springer, 1927.

This book, by Professor Lenz, head of the criminologic institute at Graz, should appeal to all scientists who are interested not only in criminologic aspects, but also in the problems of human behavior in general. It is an excellent treatise on the development of personality and especially of those traits that lead to antisocial careers. The book is divided into four parts. Part 1, which consists of three chapters, deals with definitions and the discussion of the underlying factors in the development of the personality and social relationships of individuals, with methods of study, and finally with the particular aspects of criminal biology.

The principles developed indicate a definite rejection of the older static or anatomic point of view and an adoption of the kinetic or functional view. The author approaches the problem of criminology from the point of view of the biologist, regarding the criminal as a living organism considered in its entirety, including constitution as well as the functional manifestations that proceed from it, and intricate sequences of adaptation to environmental experiences of a general or individual sort, as the case may be.

The second part discusses the development of personality. The first chapter describes the present day concepts in regard to the functional manifestations of the individual. Under this is discussed expression of the personality, the experiences, the complexes, and the unconscious. The second chapter deals with potential traits — with desire and impulses, and especially with criminal trends. Then follows a comprehensive, clear and succinct discussion of the personality problem which leads finally into a discussion of the relationship of the personality and the environmental situation to criminal acts. This is discussed in the third part of the book.

The fourth part is devoted to various types of criminals. Nowhere is the departure from the old criminal anthropology more clearly demonstrated than in this consideration of types. The types discussed are all made up of psychobiologic structure of experiences and their effects on the development of feeling of the pathologically disordered, affective functioning, and of the expressions in behavior to which they lead.

The book is well illustrated throughout with case material which is worked up with the excellence that usually characterizes the work in criminology at Graz. It is a thoughtful and careful exposition of the problem of criminology in the light of the present day knowledge of the functioning of the mind.

To those familiar with the subject, some of the chapters will seem to be overcondensed, but, on the other hand, it will perhaps be appreciated by those who will wish to inform themselves on the subject without having to struggle with voluminous dissertations on individual topics. The various topics treated are sufficiently accompanied by references to literature, particularly to German literature, so that those in search of information on special points may find a full discussion. The value of the book is further enhanced by a good index. The student of criminology who is able to read German will hardly fail to find this a desirable book for his library.

NORMALE UND PATHOLOGISCHE ANATOMIE UND HISTOLOGIE DES GROSSHIRNS. By PROF. DR. A. JAKOB (Hamburg). Price, 57 gold marks. Pp. 457 with 270 illustrations. Leipzig and Wien: Franz Deuticke, 1927. Vol. 1.

This is the first volume of a "Handbuch der Psychiatrie" under the editorial management of Professor G. Aschaffenburg. It is also the first volume of Jakob's work. The book is one of the best and most complete summaries of what we know today of the minute structure of the brain and the changes that may occur. The subjects are taken up systematically. In the first chapter, under morphology, the basic factors in ontogenesis and phylogenesis are briefly but well discussed. General considerations about the brain are also taken up under this heading and in particular one subdivision considers the weight of the brain and convolutional pattern in the brains of normal and abnormal men.

In the second chapter the microscopic structure of the end-brain is discussed. Here the cyto-architecture and the myelo-architecture is one of the high spots of this work. All that is new is considered and all of the old that

has withstood the test of time. A consideration of some of the features in Economo and Koskina's new book is inserted. The various regions of the brain are featured. The reviewer knows of no one who is better able to discuss this phase of the subject than Jakob.

In the third chapter the normal histology is thoroughly reviewed. This includes a consideration of the ganglion cell, nerve fiber, neuroglia and blood vessels. Here, for the first time, the most recent teaching of the Spanish school under Cajal's leadership appears in book form.

In the fourth chapter we are introduced to the changes that may occur in the various nervous system elements, beginning with ganglion cells, and going on into nerve fibers and the neurologia. Jakob's pioneer work on secondary degeneration of nerve fibers forms the basis for the part on the changes in the nerve fibers. It still maintains the unique position of being the best work on that subject.

In the sixth chapter, degeneration products, including pigment, calcium and hyaline, are outlined.

The seventh chapter gives an excellent summary of the changes that occur in the membranes and blood vessel apparatus. Here the work that has recently been published by some of Jakob's co-workers is included. The distinction between vessel changes as a result of age and those due to syphilis is brought out clearly.

The final chapter gives some histologic symptom complexes, such as necrosis, softening, scar formation and inflammation.

As is usual with German monographs, there is an exhaustive reference to the literature, which increases the value of the work ten-fold. All in all the book is destined to be one of the standbys in neurologic literature. As stated in the preface most of the subjects discussed are from personal contact with the material, either by Jakob himself or by one of the many men who have worked in his well equipped laboratory. The illustrations are excellent, and the publishers deserve special credit for their part in the work.

THE CONQUEST OF DISEASE. By THURMAN B. RICE, A.M., M.D., Assistant Professor of Sanitary Science, Indiana University School of Medicine. Pp. 363. New York: The Macmillan Company, 1927.

This book was prepared with three purposes in mind: first, to set forth the most recent scientific information concerning the transmissible diseases to the end that these diseases may be controlled or perhaps ultimately eradicated; second, to make the subject interesting, if possible, to the general reader, and to such persons and students as may need to study the subject, and, third, to emphasize the great advances that have already been made through scientific methods by comparing the past with the present. It is the author's firm conviction that the complete conquest of transmissible diseases waits as much on the intelligent appreciation of the facts by the laity as on the advances in research made by the medical profession. Confidence in the methods and motives of science is a most important asset to the people of the modern world, and in no field is its value more clearly demonstrated than in the conquest of disease.

A careful review has shown that the author has fulfilled these purposes amply, and the book can be highly recommended, not only to the laity but also to the medical profession, as setting forth briefly, clearly and in an interesting manner the subjects considered.

DELUSION AND BELIEF. By CHARLES MACFIE CAMPBELL, M.D., Professor in Psychiatry in Harvard Medical School. Price, $1.50. Pp. 80. Cambridge: Harvard University Press, 1926.

In this little book Dr. Campbell says just what he wants to say and just what he ought to say, and he says it attractively. The book is intended for a wide audience, but is full of interest for the physician and the medical student. "The medical profession now boasts proudly of the quantitative addition it has made to human life; the time may come when it will point with equal pride to measures which have added to the quality of human life." In a discussion of the much neglected topic of what the patient is trying to do by means of a delusion, Dr. Campbell discusses how different groups of people behave under the stress of bereavement, unsatisfied love, and longing for children and for power. His illustrations range from Tennyson, Queen Victoria and Joseph Smith to such men of science as Wallace and Darwin. The ways in which we are thrown back on primitive habits of thinking, and on inferior beliefs about health and other matters, are effectively put forth in a last chapter on the individual's relation to the group.

PATHOLOGIE ET METHODES D'EXAMEN DU LIQUIDE CEPHALO-RACHIDIEN. By B. BORCHEWSKY. Pp. 56. Price, 7 francs. Paris: Masson et Cie, 1926.

This little monograph takes up a few aspects only of the problems of the cerebrospinal fluid, the subject matter concerning chiefly the various groups showing meningitis. Few case reports are given and unfortunately they are not the author's. The second half of the book is the more important; in it, methods of examination of the fluid are given. The pamphlet is far from complete from the clinical point of view and only partially complete as a working manual. It therefore does not compare in usefulness with recent works, such as those by Greenfield and Carmichael, and by Pappenheim.

TEXT-BOOK OF BIOLOGICAL CHEMISTRY. By JAMES B. SUMNER, PH.D., Assistant Professor of Biological Chemistry, Cornell University. Price, $3.50. Pp. 283. New York: The Macmillan Company, 1927.

This book was prepared first and last for the elementary student and not for reference. The author has aimed to set forth as briefly and as simply as possible the principle facts and theories of biologic chemistry. A review has shown the book to be satisfactory for these purposes. Unfortunately, however, it is of only limited value to medical practitioners because it contains little discussion of the applications of biologic chemistry to medicine.

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